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Title Weighted Correlation Network Analysis

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Suggests org.Hs.eg.db, org.Mm.eg.db, infotheo, entropy, minet

LinkingTo Rcpp

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License GPL (>= 2)
```

Description Functions necessary to perform Weighted Correlation Network Analysis on high-dimensional data as originally described in Horvath and Zhang (2005) <doi:10.2202/1544-6115.1128> and Langfelder and Horvath (2008) <doi:10.1186/1471-2105-9-559>. Includes functions for rudimentary data cleaning, construction of correlation networks, module identification, summarization, and relating of variables and modules to sample traits. Also includes a number of utility functions for data manipulation and visualization.

NeedsCompilation yes

```
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accuracyMeasures	Accuracy measures for a 2x2 confusion matrix or for vectors of pre-
	dicted and observed values.

Description

The function calculates various prediction accuracy statistics for predictions of binary or quantitative (continuous) responses. For binary classification, the function calculates the error rate, accuracy, sensitivity, specificity, positive predictive value, and other accuracy measures. For quantitative prediction, the function calculates correlation, R-squared, error measures, and the C-index.

Usage

Arguments

predicted

either a a 2x2 confusion matrix (table) whose entries contain non-negative integers, or a vector of predicted values. Predicted values can be binary or quantitative (see type below). If a 2x2 matrix is given, it must have valid column and row names that specify the levels of the predicted and observed variables whose counts the matrix is giving (e.g., the function table sets the names appropriately.) If it is a 2x2 table and the table contains non-negative real (non-integer) numbers the function outputs a warning.

observed

if predicted is a vector of predicted values, this (observed) must be a vector of the same length giving the "gold standard" (or observed) values. Ignored if predicted is a 2x2 table.

type

character string specifying the type of the prediction problem (i.e., values in the predicted and observed vectors). The default "auto" decides type automatically: if predicted is a 2x2 table or if the number of unique values in the concatenation of predicted and observed is 2, the prediction problem (type) is assumed to be binary, otherwise it is assumed to be quantitative. Inconsistent specification (for example, when predicted is a 2x2 matrix and type is "quantitative") trigger errors.

levels

a 2-element vector specifying the two levels of binary variables. Only used if type is "binary" (or "auto" that results in the binary type). Defaults to either the column names of the confusion matrix (if the matrix is specified) or to the sorted unique values of observed and opredicted.

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negativeLevel the binary value (level) that corresponds to the negative outcome. Note that

the default is the second of the sorted levels (for example, if levels are 1,2, the default negative level is 2). Only used if type is "binary" (or "auto" that

results in the binary type).

positiveLevel the binary value (level) that corresponds to the positive outcome. Note that the

default is the second of the sorted levels (for example, if levels are 1,2, the default negative level is 2). Only used if type is "binary" (or "auto" that

results in the binary type).

Details

The rows of the 2x2 table tab must correspond to a test (or predicted) outcome and the columns to a true outcome ("gold standard"). A table that relates a predicted outcome to a true test outcome is also known as confusion matrix. Warning: To correctly calculate sensitivity and specificity, the positive and negative outcome must be properly specified so they can be matched to the appropriate rows and columns in the confusion table.

Interchanging the negative and positive levels swaps the estimates of the sensitivity and specificity but has no effect on the error rate or accuracy. Specifically, denote by pos the index of the positive level in the confusion table, and by neg the eindex of the negative level in the confusion table. The function then defines number of true positives=TP=tab[pos, pos], no.false positives=FP=tab[pos, neg], no.false negatives=FN=tab[neg, pos], no.true negatives=TN=tab[neg, neg]. Then Specificity=TN/(FP+TN) Sensitivity=TP/(TP+FN) NegativePredictiveValue=TN/(FN + TN) PositivePredictiveValue=TP/(TP+FP) FalsePositiveRate=1-Specificity FalseNegativeRate=1-Sensitivity Power=Sensitivity LikelihoodRatioPositive=Sensitivity / (1-Specificity) LikelihoodRatioNegative=(1-Sensitivity)/Specificity. The naive error rate is the error rate of a constant (naive) predictor that assigns the same outcome to all samples. The prediction of the naive predictor equals the most frequenly observed outcome. Example: Assume you want to predict disease status and 70 percent of the observed samples have the disease. Then the naive predictor has an error rate of 30 percent (since it only misclassifies 30 percent of the healthy individuals).

Value

Data frame with two columns:

Measure this column contais character strings that specify name of the accuracy measure.

Value this column contains the numeric estimates of the corresponding accuracy mea-

sures.

Author(s)

Steve Horvath and Peter Langfelder

References

http://en.wikipedia.org/wiki/Sensitivity_and_specificity

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Examples

```
m=100
trueOutcome=sample( c(1,2),m,replace=TRUE)
predictedOutcome=trueOutcome
# now we noise half of the entries of the predicted outcome
predictedOutcome[ 1:(m/2)] =sample(predictedOutcome[ 1:(m/2)] )
tab=table(predictedOutcome, trueOutcome)
accuracyMeasures(tab)
# Same result:
accuracyMeasures(predictedOutcome, trueOutcome)
```

addErrorBars

Add error bars to a barplot.

Description

This function adds error bars to an existing barplot.

Usage

```
addErrorBars(means, errors, two.side = FALSE)
```

Arguments

means vector of means plotted in the barplot

errors vector of standard errors (signle positive values) to be plotted.

two.side should the error bars be two-sided?

Value

None.

Author(s)

Steve Horvath and Peter Langfelder

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addGrid

Add grid lines to an existing plot.

Description

This function adds horizontal and/or vertical grid lines to an existing plot. The grid lines are aligned with tick marks.

Usage

```
addGrid(
  linesPerTick = NULL,
  linesPerTick.horiz = linesPerTick,
  linesPerTick.vert = linesPerTick,
  horiz = TRUE,
  vert = FALSE,
  col = "grey30",
  lty = 3)
```

Arguments

linesPerTick Number of lines between successive tick marks (including the line on the tick-marks themselves).

linesPerTick.horiz

Number of horizontal lines between successive tick marks (including the line on the tickmarks themselves).

linesPerTick.vert

Number of vertical lines between successive tick marks (including the line on the tickmarks themselves).

horiz Draw horizontal grid lines?
vert Draw vertical tick lines?

col Specifies color of the grid lines

1ty Specifies line type of grid lines. See par.

Details

If linesPerTick is not specified, it is set to 5 if number of tick s is 5 or less, and it is set to 2 if number of ticks is greater than 5.

Note

The function does not work whenever logarithmic scales are in use.

Author(s)

Peter Langfelder

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Examples

```
plot(c(1:10), c(1:10))
addGrid();
```

addGuideLines

Add vertical "guide lines" to a dendrogram plot

Description

Adds vertical "guide lines" to a dendrogram plot.

Usage

Arguments

The dendrogram (see hclust) to which the guide lines are to be added.
Add a guide line to every object on the dendrogram? Useful if the number of objects is relatively low.
Number of guide lines to be plotted. The lines will be equidistantly spaced.
Horizontal positions of the added guide lines. If given, overrides count.
Color of the guide lines
Line type of the guide lines. See par.
Fraction of the figure height that will separate top ends of guide lines and the merge heights of the corresponding objects.

Author(s)

Peter Langfelder

12 addTraitToMEs

addTr	aitT	OMF s	

Add trait information to multi-set module eigengene structure

Description

Adds trait information to multi-set module eigengene structure.

Usage

```
addTraitToMEs(multiME, multiTraits)
```

Arguments

multiME Module eigengenes in multi-set format. A vector of lists, one list per set. Each

list must contain an element named data that is a data frame with module eigen-

genes.

multiTraits Microarray sample trait(s) in multi-set format. A vector of lists, one list per set.

Each list must contain an element named data that is a data frame in which each

column corresponds to a trait, and each row to an individual sample.

Details

The function simply cbind's the module eigengenes and traits for each set. The number of sets and numbers of samples in each set must be consistent between multiMEs and multiTraits.

Value

A multi-set structure analogous to the input: a vector of lists, one list per set. Each list will contain a component data with the merged eigengenes and traits for the corresponding set.

Author(s)

Peter Langfelder

See Also

checkSets, moduleEigengenes

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adjacency	Calculate network adjacency	

Description

Calculates (correlation or distance) network adjacency from given expression data or from a similarity.

Usage

Arguments

datExpr	data frame containing expression data. Columns correspond to genes and rows to samples.
similarity	a (signed) similarity matrix: square, symmetric matrix with entries between -1 and 1.
selectCols	for correlation networks only (see below); can be used to select genes whose adjacencies will be calculated. Should be either a numeric vector giving the indices of the genes to be used, or a boolean vector indicating which genes are to be used.
type	network type. Allowed values are (unique abbreviations of) "unsigned", "signed" "signed hybrid", "distance".
power	soft thresholding power.
corFnc	character string specifying the function to be used to calculate co-expression similarity for correlation networks. Defaults to Pearson correlation. Any function returning values between -1 and 1 can be used.
corOptions	character string or a list specifying additional arguments to be passed to the function given by corFnc. Use "use = 'p', method = 'spearman'" or, equivalently, list(use = 'p', method = 'spearman') to obtain Spearman correlation.

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weights optional observation weights for datExpr to be used in correlation calculation.

A matrix of the same dimensions as datExpr, containing non-negative weights.

Only used with Pearson correlation.

distFnc character string specifying the function to be used to calculate co-expression

similarity for distance networks. Defaults to the function dist. Any function

returning non-negative values can be used.

distOptions character string or a list specifying additional arguments to be passed to the

function given by distFnc. For example, when the function dist is used, the argument method can be used to specify various ways of computing the distance.

weightArgNames character vector of length 2 giving the names of the arguments to corFnc that

represent weights for variable x and y. Only used if weights are non-NULL.

Details

The argument type determines whether a correlation (type one of "unsigned", "signed", "signed hybrid"), or a distance network (type equal "distance") will be calculated. In correlation networks the adajcency is constructed from correlations (values between -1 and 1, with high numbers meaning high similarity). In distance networks, the adjacency is constructed from distances (nonnegative values, high values mean low similarity).

The function calculates the similarity of columns (genes) in datExpr by calling the function given in corFnc (for correlation networks) or distFnc (for distance networks), transforms the similarity according to type and raises it to power, resulting in a weighted network adjacency matrix. If selectCols is given, the corFnc function will be given arguments (datExpr, datExpr[selectCols], ...); hence the returned adjacency will have rows corresponding to all genes and columns corresponding to genes selected by selectCols.

Correlation and distance are transformed as follows: for type = "unsigned", adjacency = |corl^power; for type = "signed", adjacency = (0.5 * (1+cor))^power; for type = "signed hybrid", adjacency = cor^power if cor>0 and 0 otherwise; and for type = "distance", adjacency = (1-(dist/max(dist))^2)^power.

The function adjacency.fromSimilarity inputs a similarity matrix, that is it skips the correlation calculation step but is otherwise identical.

Value

Adjacency matrix of dimensions ncol(datExpr) times ncol(datExpr) (or the same dimensions as similarity). If selectCols was given, the number of columns will be the length (if numeric) or sum (if boolean) of selectCols.

Note

When calculated from the datExpr, the network is always calculated among the columns of datExpr irrespective of whether a correlation or a distance network is requested.

Author(s)

Peter Langfelder and Steve Horvath

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References

Bin Zhang and Steve Horvath (2005) A General Framework for Weighted Gene Co-Expression Network Analysis, Statistical Applications in Genetics and Molecular Biology, Vol. 4 No. 1, Article 17

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

adjacency.polyReg

Adjacency matrix based on polynomial regression

Description

adjacency.polyReg calculates a network adjacency matrix by fitting polynomial regression models to pairs of variables (i.e. pairs of columns from datExpr). Each polynomial fit results in a model fitting index R.squared. Thus, the n columns of datExpr result in an n x n dimensional matrix whose entries contain R.squared measures. This matrix is typically non-symmetric. To arrive at a (symmetric) adjacency matrix, one can specify different symmetrization methods with symmetrizationMethod.

Usage

adjacency.polyReg(datExpr, degree=3, symmetrizationMethod = "mean")

Arguments

data frame containing numeric variables. Example: Columns may correspond

to genes and rows to observations (samples).

degree the degree of the polynomial. Must be less than the number of unique points.

symmetrizationMethod

character string (eg "none", "min", "max", "mean") that specifies the method used

to symmetrize the pairwise model fitting index matrix (see details).

Details

A network adjacency matrix is a symmetric matrix whose entries lie between 0 and 1. It is a special case of a similarity matrix. Each variable (column of datExpr) is regressed on every other variable, with each model fitting index recorded in a square matrix. Note that the model fitting index of regressing variable x and variable y is usually different from that of regressing y on x. From the polynomial regression model glm(y ~ poly(x,degree)) one can calculate the model fitting index R.squared(y,x). R.squared(y,x) is a number between 0 and 1. The closer it is to 1, the better the polynomial describes the relationship between x and y and the more significant is the pairwise relationship between the 2 variables. One can also reverse the roles of x and y to arrive at a model fitting index R.squared(x,y). If degree>1 then R.squared(x,y) is typically different from R.squared(y,x). Assume a set of n variables x1,...,xn (corresponding to the columns of datExpr then one can define R.squared(xi,xj). The model fitting indices for the elements of an n x n dimensional matrix (R.squared(ij)). symmetrizationMethod implements the following symmetrization methods:

A.min(ij)=min(R.squared(ij),R.squared(ji)), A.ave(ij)=(R.squared(ij)+R.squared(ji))/2, A.max(ij)=max(R.squared(ij),R.squared(ij)

Value

An adjacency matrix of dimensions ncol(datExpr) times ncol(datExpr).

Author(s)

Lin Song, Steve Horvath

References

Song L, Langfelder P, Horvath S Avoiding mutual information based co-expression measures (to appear).

Horvath S (2011) Weighted Network Analysis. Applications in Genomics and Systems Biology. Springer Book. ISBN: 978-1-4419-8818-8

See Also

For more information about polynomial regression, please refer to functions poly and glm

Examples

```
#Simulate a data frame datE which contains 5 columns and 50 observations
m = 50
x1=rnorm(m)
r=.5; x2=r*x1+sqrt(1-r^2)*rnorm(m)
r=.3; x3=r*(x1-.5)^2+sqrt(1-r^2)*rnorm(m)
x4=rnorm(m)
r=.3; x5=r*x4+sqrt(1-r^2)*rnorm(m)
datE=data.frame(x1,x2,x3,x4,x5)
#calculate adjacency by symmetrizing using max
A.max=adjacency.polyReg(datE, symmetrizationMethod="max")
A.max
#calculate adjacency by symmetrizing using max
A.mean=adjacency.polyReg(datE, symmetrizationMethod="mean")
# output the unsymmetrized pairwise model fitting indices R.squared
R.squared=adjacency.polyReg(datE, symmetrizationMethod="none")
R.squared
```

adjacency.splineReg

Calculate network adjacency based on natural cubic spline regression

Description

adjacency.splineReg calculates a network adjacency matrix by fitting spline regression models to pairs of variables (i.e. pairs of columns from datExpr). Each spline regression model results in a fitting index R.squared. Thus, the n columns of datExpr result in an n x n dimensional matrix whose entries contain R.squared measures. This matrix is typically non-symmetric. To arrive at a (symmetric) adjacency matrix, one can specify different symmetrization methods with symmetrizationMethod.

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Usage

```
adjacency.splineReg(
  datExpr,
  df = 6-(nrow(datExpr)<100)-(nrow(datExpr)<30),
  symmetrizationMethod = "mean",
  ...)</pre>
```

Arguments

date frame containing numeric variables. Example: Columns may correspond

to genes and rows to observations (samples).

df degrees of freedom in generating natural cubic spline. The default is as follows:

if nrow(datExpr)>100 use 6, if nrow(datExpr)>30 use 4, otherwise use 5.

symmetrizationMethod

character string (eg "none", "min", "max", "mean") that specifies the method used

to symmetrize the pairwise model fitting index matrix (see details).

... other arguments from function ns

Details

A network adjacency matrix is a symmetric matrix whose entries lie between 0 and 1. It is a special case of a similarity matrix. Each variable (column of datExpr) is regressed on every other variable, with each model fitting index recorded in a square matrix. Note that the model fitting index of regressing variable x and variable y is usually different from that of regressing y on x. From the spline regression model glm($y \sim ns(x, df)$) one can calculate the model fitting index R.squared(y,x). R.squared(y,x) is a number between 0 and 1. The closer it is to 1, the better the spline regression model describes the relationship between x and y and the more significant is the pairwise relationship between the 2 variables. One can also reverse the roles of x and y to arrive at a model fitting index R.squared(x,y). R.squared(x,y) is typically different from R.squared(y,x). Assume a set of n variables x1,...,xn (corresponding to the columns of datExpr) then one can define R.squared(xi,xj). The model fitting indices for the elements of an n x n dimensional matrix (R.squared(ij)). symmetrizationMethod implements the following symmetrization methods:

A.min(ij)=min(R.squared(ij),R.squared(ji)), A.ave(ij)=(R.squared(ij)+R.squared(ji))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij)+R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squared(ij),R.squared(ij))/2, A.max(ij)=max(R.squared(ij),R.squ

Value

An adjacency matrix of dimensions ncol(datExpr) times ncol(datExpr).

Author(s)

Lin Song, Steve Horvath

References

Song L, Langfelder P, Horvath S Avoiding mutual information based co-expression measures (to appear).

Horvath S (2011) Weighted Network Analysis. Applications in Genomics and Systems Biology. Springer Book. ISBN: 978-1-4419-8818-8

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See Also

```
ns, glm
```

Examples

```
#Simulate a data frame datE which contains 5 columns and 50 observations
m=50
x1=rnorm(m)
r=.5; x2=r*x1+sqrt(1-r^2)*rnorm(m)
r=.3; x3=r*(x1-.5)^2+sqrt(1-r^2)*rnorm(m)
x4=rnorm(m)
r=.3; x5=r*x4+sqrt(1-r^2)*rnorm(m)
datE=data.frame(x1,x2,x3,x4,x5)
#calculate adjacency by symmetrizing using max
A.max=adjacency.splineReg(datE, symmetrizationMethod="max")
A.max
#calculate adjacency by symmetrizing using max
A.mean=adjacency.splineReg(datE, symmetrizationMethod="mean")
A.mean
# output the unsymmetrized pairwise model fitting indices R.squared
R.squared=adjacency.splineReg(datE, symmetrizationMethod="none")
R.squared
```

AFcorMI

Prediction of Weighted Mutual Information Adjacency Matrix by Correlation

Description

AFcorMI computes a predicted weighted mutual information adjacency matrix from a given correlation matrix.

Usage

```
AFcorMI(r, m)
```

Arguments

r a symmetric correlation matrix with values from -1 to 1.

m number of observations from which the correlation was calcuated.

Details

This function is a one-to-one prediction when we consider correlation as unsigned. The prediction corresponds to the AdjacencyUniversalVersion2 discussed in the help file for the function mutualInfoAdjacency. For more information about the generation and features of the predicted mutual information adjacency, please refer to the function mutualInfoAdjacency.

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Value

A matrix with the same size as the input correlation matrix, containing the predicted mutual information of type AdjacencyUniversalVersion2.

Author(s)

Steve Horvath, Lin Song, Peter Langfelder

See Also

```
mutualInfoAdjacency
```

Examples

```
#Simulate a data frame datE which contains 5 columns and 50 observations
m=50
x1=rnorm(m)
r=.5; x2=r*x1+sqrt(1-r^2)*rnorm(m)
r=.3; x3=r*(x1-.5)^2+sqrt(1-r^2)*rnorm(m)
x4=rnorm(m)
r=.3; x5=r*x4+sqrt(1-r^2)*rnorm(m)
datE=data.frame(x1,x2,x3,x4,x5)
#calculate predicted AUV2
cor.data=cor(datE, use="p")
AUV2=AFcorMI(r=cor.data, m=nrow(datE))
```

alignExpr

Align expression data with given vector

Description

Multiplies genes (columns) in given expression data such that their correlation with given reference vector is non-negative.

Usage

```
alignExpr(datExpr, y = NULL)
```

Arguments

datExpr expression data to be aligned. A data frame with columns corresponding to genes and rows to samples.

y reference vector of length equal the number of samples (rows) in datExpr

Details

The function basically multiplies each column in datExpr by the sign of its correlation with y. If y is not given, the first column in datExpr will be used as the reference vector.

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Value

A data frame containing the aligned expression data, of the same dimensions as the input data frame.

Author(s)

Steve Horvath and Peter Langfelder

allocateJobs

Divide tasks among workers

Description

This function calculates an even splitting of a given number of tasks among a given number of workers (threads).

Usage

```
allocateJobs(nTasks, nWorkers)
```

Arguments

nTasks

number of tasks to be divided

nWorkers

number of workers

Details

Tasks are labeled consecutively 1,2,..., nTasks. The tasks are split in contiguous blocks as evenly as possible.

Value

A list with one component per worker giving the task indices to be worked on by each worker. If there are more workers than tasks, the tasks for the extra workers are 0-length numeric vectors.

Author(s)

Peter Langfelder

Examples

```
allocateJobs(10, 3);
allocateJobs(2,4);
```

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allowWGCNAThreads

Allow and disable multi-threading for certain WGCNA calculations

Description

These functions allow and disable multi-threading for WGCNA calculations that can optionally be multi-threaded, which includes all functions using cor or bicor functions.

Usage

```
allowWGCNAThreads(nThreads = NULL)
enableWGCNAThreads(nThreads = NULL)
disableWGCNAThreads()
WGCNAnThreads()
```

Arguments

nThreads

Number of threads to allow. If not given, the number of processors online (as reported by system configuration) will be used. There appear to be some cases where the automatically-determined number is wrong; please check the output to see that the number of threads makes sense. Except for testing and/or torturing your system, the number of threads should be no more than the number of actual processors/cores.

Details

allowWGCNAThreads enables parallel calculation within the compiled code in WGCNA, principally for calculation of correlations in the presence of missing data. This function is now deprecated; use enablewGCNAThreads instead.

enableWGCNAThreads enables parallel calculations within user-level R functions as well as within the compiled code, and registers an appropriate parallel calculation back-end for the operating system/platform.

disablewGCNAThreads disables parallel processing.

WGCNAnThreads returns the number of threads (parallel processes) that WGCNA is currently configured to run with.

Value

allowWGCNAThreads, enableWGCNAThreads, and disableWGCNAThreads return the maximum number of threads WGCNA calculations will be allowed to use.

Note

Multi-threading within compiled code is not available on Windows; R code parallelization works on all platforms.

Author(s)

Peter Langfelder

automaticNetworkScreening

One-step automatic network gene screening

Description

This function performs gene screening based on a given trait and gene network properties

Usage

```
automaticNetworkScreening(
   datExpr,
   y,
   power = 6,
   networkType = "unsigned",
   detectCutHeight = 0.995,
   minModuleSize = min(20, ncol(as.matrix(datExpr))/2),
   datME = NULL,
   getQValues = TRUE,
   ...)
```

Arguments

data frame containing the expression data, columns corresponding to genes and

rows to samples

y vector containing trait values for all samples in datExpr power soft thresholding power used in network construction

networkType character string specifying network type. Allowed values are (unique abbrevia-

tions of) "unsigned", "signed", "hybrid".

detectCutHeight

cut height of the gene hierarchical clustering dendrogram. See cutreeDynamic

for details.

minModuleSize minimum module size to be used in module detection procedure.

datME optional specification of module eigengenes. A data frame whose columns are

the module eigengenes. If given, module analysis will not be performed.

getQValues logical: should q-values (local FDR) be calculated?

... other arguments to the module identification function blockwiseModules

Details

Network screening is a method for identifying genes that have a high gene significance and are members of important modules at the same time. If datME is given, the function calls networkScreening with the default parameters. If datME is not given, module eigengenes are first calculated using network analysis based on supplied parameters.

Value

A list with the following components:

networkScreening

 $a \ data \ frame \ containing \ results \ of \ the \ network \ screening \ procedure. \ See \ network Screening$

for more details.

datME calculated module eigengenes (or a copy of the input datME, if given).

hubGeneSignificance

hub gene significance for all calculated modules. See hubGeneSignificance.

Author(s)

Steve Horvath

See Also

networkScreening, hubGeneSignificance, networkScreening, cutreeDynamic

 $automatic {\tt NetworkScreeningGS}$

One-step automatic network gene screening with external gene significance

Description

This function performs gene screening based on external gene significance and their network properties.

Usage

```
automaticNetworkScreeningGS(
    datExpr, GS,
    power = 6, networkType = "unsigned",
    detectCutHeight = 0.995, minModuleSize = min(20, ncol(as.matrix(datExpr))/2),
    datME = NULL)
```

Arguments

data frame containing the expression data, columns corresponding to genes and

rows to samples

GS vector containing gene significance for all genes given in datExpr

power soft thresholding power used in network construction

networkType character string specifying network type. Allowed values are (unique abbrevia-

tions of) "unsigned", "signed", "hybrid".

detectCutHeight

cut height of the gene hierarchical clustering dendrogram. See cutreeDynamic

for details.

minModuleSize minimum module size to be used in module detection procedure.

datME optional specification of module eigengenes. A data frame whose columns are

the module eigengenes. If given, module analysis will not be performed.

Details

Network screening is a method for identifying genes that have a high gene significance and are members of important modules at the same time. If datME is given, the function calls networkScreeningGS with the default parameters. If datME is not given, module eigengenes are first calculated using network analysis based on supplied parameters.

Value

A list with the following components:

networkScreening

a data frame containing results of the network screening procedure. See networkScreeningGS

for more details.

datME calculated module eigengenes (or a copy of the input datME, if given).

hubGeneSignificance

hub gene significance for all calculated modules. See hubGeneSignificance.

Author(s)

Steve Horvath

See Also

networkScreening, hubGeneSignificance, networkScreening, cutreeDynamic

BD.getData 25

BD.getData	Various basic operations on BlockwiseData objects.	

Description

These functions implement basic operations on BlockwiseData objects. Blockwise here means that the data is too large to be loaded or processed in one piece and is therefore split into blocks that can be handled one by one in a divide-and-conquer manner.

Usage

```
BD.actualFileNames(bwData)
BD.nBlocks(bwData)
BD.blockLengths(bwData)
BD.getMetaData(bwData, blocks = NULL, simplify = TRUE)
BD.getData(bwData, blocks = NULL, simplify = TRUE)
BD.checkAndDeleteFiles(bwData)
```

Arguments

bwData	A BlockwiseData object.
blocks	Optional vector of integers specifying the blocks on which to execute the operation.
simplify	Logical: if the blocks argument above is of length 1, should the returned list be simplified by removing the redundant outer list structure?

Details

Several functions in this package use the concept of blockwise, or "divide-and-conquer", analysis. The BlockwiseData class is meant to hold the blockwise data, or all necessary information about blockwise data that is saved in disk files.

Value

lue				
	BD.actualFileNames			
		returns a vector of character strings giving the file names in which the files are saved, or NULL if the data are held in-memory.		
	BD.nBlocks	returns the number of blocks in the input object.		
	BD.blockLengths			
		returns the block lengths (results of applying length to the data in each block).		
	BD.getMetaData	returns a list with one component per block. Each component is in turn a list containing the stored meta-data for the corresponding block. If blocks is of length 1 and simplify is TRUE, the outer (redundant) list is removed.		
	BD.getData	returns a list with one component per block. Each component is in turn a list containing the stored data for the corresponding block. If blocks is of length 1 and simplify is TRUE, the outer (redundant) list is removed.		

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```
BD.checkAndDeleteFiles
```

deletes the files referenced in the input bwData if they exist.

Warning

The definition of BlockwiseData and the functions here should be considered experimental and may change in the future.

Author(s)

Peter Langfelder

See Also

```
Definition of and other functions on BlockwiseData:
```

```
newBlockwiseData for creating new BlockwiseData objects;
mergeBlockwiseData for merging blockwise data structure;
addBlockToBlockwiseData for adding a new block to existing blockwise data;
```

bicor

Biweight Midcorrelation

Description

Calculate biweight midcorrelation efficiently for matrices.

Usage

```
bicor(x, y = NULL,
    robustX = TRUE, robustY = TRUE,
    use = "all.obs",
    maxPOutliers = 1,
    quick = 0,
    pearsonFallback = "individual",
    cosine = FALSE,
    cosineX = cosine,
    cosineY = cosine,
    nThreads = 0,
    verbose = 0, indent = 0)
```

Arguments

```
x a vector or matrix-like numeric object
y a vector or matrix-like numeric object
robustX use robust calculation for x?
robustY use robust calculation for y?
```

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specifies handling of NAs. One of (unique abbreviations of) "all.obs", "pairuse wise.complete.obs".

maxPOutliers specifies the maximum percentile of data that can be considered outliers on

either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar (but not equal to) Pear-

son correlation.

quick real number between 0 and 1 that controls the handling of missing data in the

calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation

manner (as if the corresponding robust option was set to FALSE).

cosine logical: calculate cosine biweight midcorrelation? Cosine bicorrelation is simi-

lar to standard bicorrelation but the median subtraction is not performed.

cosineX logical: use the cosine calculation for x? This setting does not affect y and can

be used to give a hybrid cosine-standard bicorrelation.

cosineY logical: use the cosine calculation for y? This setting does not affect x and can

be used to give a hybrid cosine-standard bicorrelation.

nThreads non-negative integer specifying the number of parallel threads to be used by cer-

> tain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads. Note that this option does not affect what is usually the most expensive part of the calculation, namely the matrix multiplication. The matrix multiplication is carried out by BLAS routines provided by R; these can

be sped up by installing a fast BLAS and making R use it.

verbose if non-zero, the underlying C function will print some diagnostics.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function implements biweight midcorrelation calculation (see references). If y is not supplied, midcorrelation of columns of x will be calculated; otherwise, the midcorrelation between columns of x and y will be calculated. Thus, bicor(x) is equivalent to bicor(x,x) but is more efficient.

The options robustX, robustY allow the user to revert the calculation to standard correlation calculation. This is important, for example, if any of the variables is binary (or, more generally, discrete) 28 bicor

as in such cases the robust methods produce meaningless results. If both robustX, robustY are set to FALSE, the function calculates the standard Pearson correlation (but is slower than the function cor).

The argument quick specifies the precision of handling of missing data in the correlation calculations. Value quick = 0 will cause all calculations to be executed accurately, which may be significantly slower than calculations without missing data. Progressively higher values will speed up the calculations but introduce progressively larger errors. Without missing data, all column meadians and median absolute deviations (MADs) can be pre-calculated before the covariances are calculated. When missing data are present, exact calculations require the column medians and MADs to be calculated for each covariance. The approximate calculation uses the pre-calculated median and MAD and simply ignores missing data in the covariance calculation. If the number of missing data is high, the pre-calculated medians and MADs may be very different from the actual ones, thus potentially introducing large errors. The quick value times the number of rows specifies the maximum difference in the number of missing entries for median and MAD calculations on the one hand and covariance on the other hand that will be tolerated before a recalculation is triggered. The hope is that if only a few missing data are treated approximately, the error introduced will be small but the potential speedup can be significant.

The choice "all" for pearsonFallback is not fully implemented in the sense that there are rare but possible cases in which the calculation is equivalent to "individual". This may happen if the use option is set to "pairwise.complete.obs" and the missing data are arranged such that each individual mad is non-zero, but when two columns are analyzed together, the missing data from both columns may make a mad zero. In such a case, the calculation is treated as Pearson, but other columns will be treated as bicor.

Value

A matrix of biweight midcorrelations. Dimnames on the result are set appropriately.

Author(s)

Peter Langfelder

References

Peter Langfelder, Steve Horvath (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software, 46(11), 1-17. https://www.jstatsoft.org/v46/i11/

"Introduction to Robust Estimation and Hypothesis Testing", Rand Wilcox, Academic Press, 1997.

"Data Analysis and Regression: A Second Course in Statistics", Mosteller and Tukey, Addison-Wesley, 1977, pp. 203-209.

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bicorAndPvalue	Calculation of biweight midcorrelations and associated p-values
bicorAndPvalue	Calculation of biweight midcorrelations and associated p-values

Description

A faster, one-step calculation of Student correlation p-values for multiple biweight midcorrelations, properly taking into account the actual number of observations.

Usage

Arguments

x	a vector or a matrix
у	a vector or a matrix. If NULL, the correlation of columns of x will be calculated.
use	determines handling of missing data. See bicor for details.
alternative	specifies the alternative hypothesis and must be (a unique abbreviation of) one of "two.sided", "greater" or "less". the initial letter. "greater" corresponds to positive association, "less" to negative association.
	other arguments to the function bicor.

Details

The function calculates the biweight midcorrelations of a matrix or of two matrices and the corresponding Student p-values. The output is not as full-featured as cor.test, but can work with matrices as input.

Value

A list with the following components, each a marix:

bicor	the calculated correlations
p	the Student p-values corresponding to the calculated correlations
Z	Fisher transform of the calculated correlations
t	Student t statistics of the calculated correlations
n0bs	Numbers of observations for the correlation, p-values etc.

Author(s)

Peter Langfelder and Steve Horvath

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References

Peter Langfelder, Steve Horvath (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software, 46(11), 1-17. https://www.jstatsoft.org/v46/i11/

See Also

```
bicor for calculation of correlations only;
cor.test for another function for significance test of correlations
```

Examples

```
# generate random data with non-zero correlation
set.seed(1);
a = rnorm(100);
b = rnorm(100) + a;
x = cbind(a, b);
# Call the function and display all results
bicorAndPvalue(x)
# Set some components to NA
x[c(1:4), 1] = NA
corAndPvalue(x)
# Note that changed number of observations.
```

bicovWeights

Weights used in biweight midcovariance

Description

Calculation of weights and the intermediate weight factors used in the calculation of biweight mid-covariance and midcorrelation. The weights are designed such that outliers get smaller weights; the weights become zero for data points more than 9 median absolute deviations from the median.

Usage

```
bicovWeights(
    x,
    pearsonFallback = TRUE,
    maxPOutliers = 1,
    outlierReferenceWeight = 0.5625,
    defaultWeight = 0)

bicovWeightFactors(
    x,
    pearsonFallback = TRUE,
    maxPOutliers = 1,
    outlierReferenceWeight = 0.5625,
```

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```
defaultFactor = NA)
bicovWeightsFromFactors(
   u,
   defaultWeight = 0)
```

Arguments

u

x A vector or a two-dimensional array (matrix or data frame). If two-dimensional, the weights will be calculated separately on each column.

A vector or matrix of weight factors, usually calculated by bicovWeightFactors.

pearsonFallback

Logical: if the median absolute deviation is zero, should standard deviation be

substituted?

maxPOutliers Optional specification of the maximum proportion of outliers, i.e., data with

weights equal to outlierReferenceWeight below.

outlierReferenceWeight

A number between 0 and 1 specifying what is to be considered an outlier when

calculating the proportion of outliers.

defaultWeight Value used for weights that correspond to a finite x but the weights themselves

would not be finite, for example, when a column in x is constant.

defaultFactor Value used for factors that correspond to a finite x but the weights themselves

would not be finite, for example, when a column in x is constant.

Details

These functions are based on Equations (1) and (3) in Langfelder and Horvath (2012). The weight factor is denoted u in that article.

Langfelder and Horvath (2012) also describe the Pearson fallback and maximum proportion of outliers in detail. For a full discussion of the biweight midcovariance and midcorrelation, see Wilcox (2005).

Value

A vector or matrix of the same dimensions as the input x giving the bisquare weights (bicovWeights and bicovWeightsFromFactors) or the bisquare factors (bicovWeightFactors).

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering Journal of Statistical Software 46(11) 1-17 PMID: 23050260 PMCID: PMC3465711 Wilcox RR (2005). Introduction to Robust Estimation and Hypothesis Testing. 2nd edition. Academic Press, Section 9.3.8, page 399 as well as Section 3.12.1, page 83.

See Also

bicor

Examples

```
x = rnorm(100);
x[1] = 10;
plot(x, bicovWeights(x));
```

binarizeCategoricalColumns

Turn categorical columns into sets of binary indicators

Description

Given a data frame with (some) categorical columns, this function creates a set of indicator variables for the various possible sets of levels.

Usage

```
binarizeCategoricalColumns(
   data,
   convertColumns = NULL,
   considerColumns = NULL,
   maxOrdinalLevels = 3,
   levelOrder = NULL,
   minCount = 3,
   val1 = 0, val2 = 1,
   includePairwise = FALSE,
   includeLevelVsAll = TRUE,
   dropFirstLevelVsAll = TRUE,
   dropUninformative = TRUE,
   includePrefix = TRUE,
   prefixSep = ".",
   nameForAll = "all",
   levelSep = NULL,
   levelSep.pairwise = if (length(levelSep)==0) ".vs." else levelSep,
   levelSep.vsAll = if (length(levelSep)==0)
              (if (nameForAll=="") "" else ".vs.") else levelSep,
   checkNames = FALSE,
   includeLevelInformation = FALSE)
binarizeCategoricalColumns.pairwise(
  maxOrdinalLevels = 3,
   convertColumns = NULL,
   considerColumns = NULL,
```

```
levelOrder = NULL,
   val1 = 0, val2 = 1,
   includePrefix = TRUE,
   prefixSep = ".",
   levelSep = ".vs."
   checkNames = FALSE)
binarizeCategoricalColumns.forRegression(
   data.
   maxOrdinalLevels = 3,
   convertColumns = NULL,
   considerColumns = NULL,
   levelOrder = NULL,
   val1 = 0, val2 = 1,
   includePrefix = TRUE,
   prefixSep = ".",
   checkNames = TRUE)
binarizeCategoricalColumns.forPlots(
   maxOrdinalLevels = 3,
   convertColumns = NULL,
   considerColumns = NULL,
   levelOrder = NULL,
   val1 = 0, val2 = 1,
   includePrefix = TRUE,
   prefixSep = ".",
   checkNames = TRUE)
```

Arguments

data

A data frame.

convertColumns Optional character vector giving the column names of the columns to be converted. See maxOrdinalLevels below.

considerColumns

Optional character vector giving the column names of columns that should be looked at and possibly converted. If not given, all columns will be considered. See maxOrdinalLevels below.

maxOrdinalLevels

When convertColumns above is NULL, the function looks at all columns in considerColumns and converts all non-numeric columns and those numeric columns that have at most maxOrdinalLevels unique values. A column is considered numeric if its storage mode is numeric or if it is character and all entries with the expception of "NA", "NULL" and "NO DATA" represent valid numbers.

levelOrder

Optional list giving the ordering of levels (unique values) in each of the converted columns. Best used in conjunction with convertColumns.

minCount

Levels of x for which there are fewer than minCount elements will be ignored.

val1 Value for the lower level in binary comparisons.

val2 Value for the higher level in binary comparisons.

includePairwise

Logical: should pairwise binary indicators be included? For each pair of levels, the indicator is val1 for the lower level (earlier in levelOrder), val2 for the higher level and NA otherwise.

includeLevelVsAll

Logical: should binary indicators for each level be included? The indicator is val2 where x equals the level and val1 otherwise.

dropFirstLevelVsAll

Logical: should the column representing first level vs. all be dropped? This makes the resulting matrix of indicators usable for regression models.

dropUninformative

Logical: should uninformative (constant) columns be dropped?

includePrefix Logical: should the column name of the binarized column be included in column

names of the output? See details.

prefixSep Separator of column names and level names in column names of the output. See

details.

nameForAll Character string that represents "all others" in the column names of indicators

of level vs. all others.

levelSep Separator for levels to be used in column names of the output. If NULL, pairwise

and level vs. all indicators will use different level separators set by levelSep.pairwise

and levelSep.vsAll.

levelSep.pairwise

Separator for levels to be used in column names for pairwise indicators in the

output.

levelSep.vsAll Separator for levels to be used in column names for level vs. all indicators in the

output.

checkNames Logical: should the names of the output be made into syntactically correct R

language names?

includeLevelInformation

Logical: should information about which levels are represented by which columns

be included in the attributes of the output?

Details

binarizeCategoricalColumns is the most general function, the rest are convenience wrappers that set some of the options to achieve the following:

binarizeCategoricalColumns.pairwise returns only pairwise (level vs. level) binary indicators.

binarizeCategoricalColumns.forRegression returns only level vs. all others binary indicators, with the first (according to levelOrder) level vs. all removed. This is essentially the same as would be returned by model.matrix except for the column representing intercept.

binarizeCategoricalColumns.forPlots returns only level vs. all others binary indicators and keeps them all.

The columns to be converted are identified as follows. If considerColumns is given, columns not contained in it will not be converted, even if they are included in convertColumns.

If convertColumns is given, those columns will be converted (except any not contained in non-empty considerColumns). If convertColumns is NULL, the function converts columns that are not numeric (as reported by is.numeric) and those numeric columns that have at most maxOrdinalValues unique non-missing values.

The function creates two types of indicators. The first is one level (unique value) of x vs. all others, i.e., for a given level, the indicator is val2 (usually 1) for all elements of x that equal the level, and val1 (usually 0) otherwise. Column names for these indicators are the concatenation of namePrefix, the level, nameSep and nameForAll. The level vs. all indicators are created for all levels that have at least minCounts samples, are present in levelOrder (if it is non-NULL) and are not included in ignore.

The second type of indicator encodes binary comparisons. For each pair of levels (both with at least minCount samples), the indicator is val2 (usually 1) for the higher level and val1 (usually 0) for the lower level. The level order is given by levelOrder (which defaults to the sorted levels of x), assumed to be sorted in increasing order. All levels with at least minCount samples that are included in levelOrder and not included in ignore are included.

Internally, the function calls binarizeCategoricalVariable for each column that is converted.

Value

A data frame in which the converted columns have been replaced by sets of binarized indicators. When includeLevelInformation is TRUE, the attribute includedLevels is a table with one column per output column and two rows, giving the two levels (unique values of x) represented by the column.

Author(s)

Peter Langfelder

Examples

binarizeCategoricalVariable

Turn a categorical variable into a set of binary indicators

Description

Given a categorical variable, this function creates a set of indicator variables for the various possible sets of levels.

Usage

```
binarizeCategoricalVariable(
   х,
   levelOrder = NULL,
   ignore = NULL,
   minCount = 3,
   val1 = 0, val2 = 1,
   includePairwise = TRUE,
   includeLevelVsAll = FALSE,
   dropFirstLevelVsAll = FALSE,
   dropUninformative = TRUE,
   namePrefix = "",
   levelSep = NULL,
   nameForAll = "all",
   levelSep.pairwise = if (length(levelSep)==0) ".vs." else levelSep,
   levelSep.vsAll = if (length(levelSep)==0)
                       (if (nameForAll=="") "" else ".vs.") else levelSep,
   checkNames = FALSE,
   includeLevelInformation = TRUE)
```

Arguments

x A vector with categorical values.

levelOrder Optional specification of the levels (unique values) of x. Defaults to sorted

unique values of x, but can be used to only include a subset of the existing

levels as well as to specify the order of the levels in the output variables.

ignore Optional specification of levels of x that are to be ignored. Note that the levels

are ignored only when deciding which variables to include in the output; the samples with these values of x will be included in "all" in indicators of level vs.

all others.

minCount Levels of x for which there are fewer than minCount elements will be ignored.

val1 Value for the lower level in binary comparisons.

val 2 Value for the higher level in binary comparisons.

includePairwise

Logical: should pairwise binary indicators be included? For each pair of levels, the indicator is val1 for the lower level (earlier in levelOrder), val2 for the higher level and NA otherwise.

includeLevelVsAll

Logical: should binary indicators for each level be included? The indicator is val2 where x equals the level and val1 otherwise.

dropFirstLevelVsAll

Logical: should the column representing first level vs. all be dropped? This makes the resulting matrix of indicators usable for regression models.

dropUninformative

Logical: should uninformative (constant) columns be dropped?

namePrefix Prefix to be used in column names of the output.

nameForAll When naming columns that represent a level vs. all others, nameForAll will be

used to represent all others.

levelSep Separator for levels to be used in column names of the output. If NULL, pairwise

and level vs. all indicators will use different level separators set by levelSep.pairwise

and levelSep.vsAll.

levelSep.pairwise

Separator for levels to be used in column names for pairwise indicators in the

output.

levelSep.vsAll Separator for levels to be used in column names for level vs. all indicators in the

output.

checkNames Logical: should the names of the output be made into syntactically correct R

language names?

includeLevelInformation

Logical: should information about which levels are represented by which columns

be included in the attributes of the output?

Details

The function creates two types of indicators. The first is one level (unique value) of x vs. all others, i.e., for a given level, the indicator is val2 (usually 1) for all elements of x that equal the level, and val1 (usually 0) otherwise. Column names for these indicators are the concatenation of namePrefix, the level, nameSep and nameForAll. The level vs. all indicators are created for all levels that have at least minCounts samples, are present in levelOrder (if it is non-NULL) and are not included in ignore.

The second type of indicator encodes binary comparisons. For each pair of levels (both with at least minCount samples), the indicator is val2 (usually 1) for the higher level and val1 (usually 0) for the lower level. The level order is given by levelOrder (which defaults to the sorted levels of x), assumed to be sorted in increasing order. All levels with at least minCount samples that are included in levelOrder and not included in ignore are included.

Value

A matrix containing the indicators variabels, one in each column. When includeLevelInformation is TRUE, the attribute includedLevels is a table with one column per output column and two rows, giving the two levels (unique values of x) represented by the column.

Author(s)

Peter Langfelder

38 blockSize

See Also

Variations and wrappers for this function: binarizeCategoricalColumns for binarizing several columns of a matrix or data frame

Examples

```
set.seed(2);
x = sample(c("A", "B", "C"), 15, replace = TRUE);
out = binarizeCategoricalVariable(x, includePairwise = TRUE, includeLevelVsAll = TRUE);
data.frame(x, out);
attr(out, "includedLevels")
# A different naming for level vs. all columns
binarizeCategoricalVariable(x, includeLevelVsAll = TRUE, nameForAll = "");
```

blockSize

Attempt to calculate an appropriate block size to maximize efficiency of block-wise calcualtions.

Description

The function uses a rather primitive way to estimate available memory and use it to suggest a block size appropriate for the many block-by-block calculations in this package.

Usage

```
blockSize(
   matrixSize,
   rectangularBlocks = TRUE,
   maxMemoryAllocation = NULL,
   overheadFactor = 3);
```

Arguments

matrixSize

the relevant dimension (usually the number of columns) of the matrix that is to be operated on block-by-block.

rectangularBlocks

logical indicating whether the bocks of data are rectangular (of size blockSize times matrixSize) or square (of size blockSize times blockSize).

maxMemoryAllocation

maximum desired memory allocation, in bytes. Should not exceed 2GB or total installed RAM (whichever is greater) on 32-bit systems, while on 64-bit systems it should not exceed the total installed RAM. If not supplied, the available memory will be estimated internally.

overheadFactor overhead factor for the memory use by R. Recommended values are between 2 (for simple calculations) and 4 or more for complicated calculations where intermediate results (for which R must also allocate memory) take up a lot of space.

Details

Multiple functions within the WGCNA package use a divide-and-conquer (also known as block-by-block, or block-wise) approach to handling large data sets. This function is meant to assist in choosing a suitable block size, given the size of the data and the available memory.

If the entire expected result fits into the allowed memory (after taking into account the expected overhead), the returned block size will equal the input matrixSize.

The internal estimation of available memory works by returning the size of largest successfully allocated block of memory. It is hoped that this will lead to reasonable results but some operating systems may actually allocate more than is available. It is therefore preferable that the user specifies the available memory by hand.

Value

A single integer giving the suggested block size, or matrixSize if the entire calculation is expected to fit into memory in one piece.

Author(s)

Peter Langfelder

Examples

```
# Suitable blocks for handling 30,000 genes within 2GB (=2^31 bytes) of memory blockSize(30000, rectangularBlocks = TRUE, maxMemoryAllocation = 2^31)
```

blockwiseConsensusModules

Find consensus modules across several datasets.

Description

Perform network construction and consensus module detection across several datasets.

Usage

```
blockwiseConsensusModules(
    multiExpr,

# Data checking options

checkMissingData = TRUE,

# Blocking options

blocks = NULL,
    maxBlockSize = 5000,
    blockSizePenaltyPower = 5,
```

```
nPreclusteringCenters = NULL,
randomSeed = 54321,
# TOM precalculation arguments, if available
individualTOMInfo = NULL,
useIndivTOMSubset = NULL,
# Network construction arguments: correlation options
corType = "pearson",
maxPOutliers = 1,
quickCor = 0,
pearsonFallback = "individual",
cosineCorrelation = FALSE,
# Adjacency function options
power = 6,
networkType = "unsigned",
checkPower = TRUE,
replaceMissingAdjacencies = FALSE,
# Topological overlap options
TOMType = "unsigned",
TOMDenom = "min",
suppressNegativeTOM = FALSE,
# Save individual TOMs?
saveIndividualTOMs = TRUE,
individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",
# Consensus calculation options: network calibration
networkCalibration = c("single quantile", "full quantile", "none"),
# Simple quantile calibration options
calibrationQuantile = 0.95,
sampleForCalibration = TRUE, sampleForCalibrationFactor = 1000,
getNetworkCalibrationSamples = FALSE,
# Consensus definition
consensusQuantile = 0,
useMean = FALSE,
```

```
setWeights = NULL,
 # Saving the consensus TOM
 saveConsensusTOMs = FALSE,
 consensusTOMFilePattern = "consensusTOM-block.%b.RData",
 # Internal handling of TOMs
 useDiskCache = TRUE, chunkSize = NULL,
 cacheBase = ".blockConsModsCache",
 cacheDir = ".",
 # Alternative consensus TOM input from a previous calculation
 consensusTOMInfo = NULL,
 # Basic tree cut options
 # Basic tree cut options
 deepSplit = 2,
 detectCutHeight = 0.995, minModuleSize = 20,
 checkMinModuleSize = TRUE,
 # Advanced tree cut opyions
 maxCoreScatter = NULL, minGap = NULL,
 maxAbsCoreScatter = NULL, minAbsGap = NULL,
 minSplitHeight = NULL, minAbsSplitHeight = NULL,
 useBranchEigennodeDissim = FALSE,
 minBranchEigennodeDissim = mergeCutHeight,
 stabilityLabels = NULL,
 minStabilityDissim = NULL,
 pamStage = TRUE, pamRespectsDendro = TRUE,
# Gene reassignment and trimming from a module, and module "significance" criteria
 reassignThresholdPS = 1e-4,
 trimmingConsensusQuantile = consensusQuantile,
 minCoreKME = 0.5, minCoreKMESize = minModuleSize/3,
 minKMEtoStay = 0.2,
 # Module eigengene calculation options
 impute = TRUE,
 trapErrors = FALSE,
```

```
#Module merging options
equalizeQuantilesForModuleMerging = FALSE,
quantileSummaryForModuleMerging = "mean",
mergeCutHeight = 0.15,
mergeConsensusQuantile = consensusQuantile,
# Output options
numericLabels = FALSE,
# General options
nThreads = 0,
verbose = 2, indent = 0, ...)
```

Arguments

multiExpr

expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

checkMissingData

logical: should data be checked for excessive numbers of missing entries in genes and samples, and for genes with zero variance? See details.

blocks

optional specification of blocks in which hierarchical clustering and module detection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the corresponding gene belongs.

maxBlockSize

integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not exceed maxBlockSize.

blockSizePenaltyPower

number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block size is very important.

nPreclusteringCenters

number of centers to be used in the preclustering. Defaults to smaller of nGenes/20 and 100*nGenes/maxBlockSize, where nGenes is the number of genes (variables) in multiExpr.

randomSeed

integer to be used as seed for the random number generator before the function starts. If a current seed exists, it is saved and restored upon exit. If NULL is given, the function will not save and restore the seed.

individualTOMInfo

Optional data for TOM matrices in individual data sets. This object is returned by the function blockwiseIndividualTOMs. If not given, appropriate topological overlaps will be calculated using the network contruction options below.

useIndivTOMSubset

If individualTOMInfo is given, this argument allows to only select a subset of the individual set networks contained in individualTOMInfo. It should be a numeric vector giving the indices of the individual sets to be used. Note that this argument is NOT applied to multiExpr.

corType

character string specifying the correlation to be used. Allowed values are (unique abbreviations of) "pearson" and "bicor", corresponding to Pearson and bidweight midcorrelation, respectively. Missing values are handled using the pariwise.complete.obs option.

maxPOutliers

only used for corType=="bicor". Specifies the maximum percentile of data that can be considered outliers on either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar (but not equal to) Pearson correlation.

quickCor

real number between 0 and 1 that controls the handling of missing data in the calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation, if used, should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE). Has no effect for Pearson correlation. See bicor.

cosineCorrelation

logical: should the cosine version of the correlation calculation be used? The cosine calculation differs from the standard one in that it does not subtract the mean.

power

soft-thresholding power for network construction. Either a single number or a vector of the same length as the number of sets, with one power for each set.

networkType

network type. Allowed values are (unique abbreviations of) "unsigned", "signed", "signed hybrid". See adjacency.

checkPower

logical: should basic sanity check be performed on the supplied power? If you would like to experiment with unusual powers, set the argument to FALSE and proceed with caution.

replaceMissingAdjacencies

logical: should missing values in the calculation of adjacency be replaced by 0?

TOMType

one of "none", "unsigned", "signed", "signed Nowick", "unsigned 2", "signed 2" and "signed Nowick 2". If "none", adjacency will be used for clustering. See TOMsimilarityFromExpr for details.

TOMDenom

a character string specifying the TOM variant to be used. Recognized values are "min" giving the standard TOM described in Zhang and Horvath (2005),

and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results but at this time should be considered experimental.

suppressNegativeTOM

Logical: should the result be set to zero when negative? Negative TOM values can occur when TOMType is "signed Nowick".

saveIndividualTOMs

logical: should individual TOMs be saved to disk for later use?

individualTOMFileNames

character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

networkCalibration

network calibration method. One of "single quantile", "full quantile", "none" (or a unique abbreviation of one of them).

calibrationQuantile

if networkCalibration is "single quantile", topological overlaps (or adjacencies if TOMs are not computed) will be scaled such that their calibrationQuantile quantiles will agree.

sampleForCalibration

if TRUE, calibration quantiles will be determined from a sample of network similarities. Note that using all data can double the memory footprint of the function and the function may fail.

sampleForCalibrationFactor

determines the number of samples for calibration: the number is 1/calibrationQuantile * sampleForCalibrationFactor. Should be set well above 1 to ensure accuracy of the sampled quantile.

getNetworkCalibrationSamples

logical: should samples used for TOM calibration be saved for future analysis? This option is only available when sampleForCalibration is TRUE.

consensusQuantile

quantile at which consensus is to be defined. See details.

useMean logical: should the consensus be determined from a (possibly weighted) mean

across the data sets rather than a quantile?

setWeights Optional vector (one component per input set) of weights to be used for weighted

mean consensus. Only used when useMean above is TRUE.

saveConsensusTOMs

logical: should the consensus topological overlap matrices for each block be saved and returned?

consensusTOMFilePattern

character string containing the file namefiles containing the consensus topological overlaps. The tag %b will be replaced by the block number. If the resulting

file names are non-unique (for example, because the user gives a file name without a %b tag), an error will be generated. These files are standard R data files and can be loaded using the load function.

useDiskCache

should calculated network similarities in individual sets be temporarilly saved to disk? Saving to disk is somewhat slower than keeping all data in memory, but for large blocks and/or many sets the memory footprint may be too big.

chunkSize

network similarities are saved in smaller chunks of size chunkSize.

cacheBase

character string containing the desired name for the cache files. The actual file names will consists of cacheBase and a suffix to make the file names unique.

cacheDir

character string containing the desired path for the cache files.

consensusTOMInfo

optional list summarizing consensus TOM, output of consensus TOM. It contains information about pre-calculated consensus TOM. Supplying this argument replaces TOM calculation, so none of the individual or consensus TOM calculation arguments are taken into account.

deepSplit

integer value between 0 and 4. Provides a simplified control over how sensitive module detection should be to module splitting, with 0 least and 4 most sensitive. See cutreeDynamic for more details.

detectCutHeight

dendrogram cut height for module detection. See cutreeDynamic for more details.

minModuleSize

minimum module size for module detection. See cutreeDynamic for more details.

checkMinModuleSize

logical: should sanity checks be performed on minModuleSize?

maxCoreScatter maximum scatter of the core for a branch to be a cluster, given as the fraction of cutHeight relative to the 5th percentile of joining heights. See cutreeDynamic for more details.

minGap

minimum cluster gap given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. See cutreeDynamic for more details.

maxAbsCoreScatter

maximum scatter of the core for a branch to be a cluster given as absolute heights. If given, overrides maxCoreScatter. See cutreeDynamic for more details.

minAbsGap

minimum cluster gap given as absolute height difference. If given, overrides minGap. See cutreeDynamic for more details.

minSplitHeight Minimum split height given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. Branches merging below this height will automatically be merged. Defaults to zero but is used only if minAbsSplitHeight below is NULL.

minAbsSplitHeight

Minimum split height given as an absolute height. Branches merging below this height will automatically be merged. If not given (default), will be determined from minSplitHeight above.

useBranchEigennodeDissim

Logical: should branch eigennode (eigengene) dissimilarity be considered when merging branches in Dynamic Tree Cut?

minBranchEigennodeDissim

Minimum consensus branch eigennode (eigengene) dissimilarity for branches to be considerd separate. The branch eigennode dissimilarity in individual sets is simly 1-correlation of the eigennodes; the consensus is defined as quantile with probability consensusQuantile.

stabilityLabels

Optional matrix of cluster labels that are to be used for calculating branch dissimilarity based on split stability. The number of rows must equal the number of genes in multiExpr; the number of columns (clusterings) is arbitrary. See branchSplitFromStabilityLabels for details.

minStabilityDissim

Minimum stability dissimilarity criterion for two branches to be considered separate. Should be a number between 0 (essentially no dissimilarity required) and 1 (perfect dissimilarity or distinguishability based on stabilityLabels). See branchSplitFromStabilityLabels for details.

pamStage logical. If TRUE, the second (PAM-like) stage of module detection will be performed. See cutreeDynamic for more details.

pamRespectsDendro

Logical, only used when pamStage is TRUE. If TRUE, the PAM stage will respect the dendrogram in the sense an object can be PAM-assigned only to clusters that lie below it on the branch that the object is merged into. See cutreeDynamic for more details.

reassignThresholdPS

per-set p-value ratio threshold for reassigning genes between modules. See Details

trimmingConsensusQuantile

a number between 0 and 1 specifying the consensus quantile used for kME calculation that determines module trimming according to the arguments below.

(its genes are unlabeled and returned to the pool of genes waiting for mofule de-

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize genes with eigengene connectivity at least minCoreKME, the module is disbanded

tection).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose eigengene connectivity to their module eigengene is lower than

minKMEtoStay are removed from the module.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

equalizeQuantilesForModuleMerging

Logical: equalize quantiles of the module eigengene networks before module merging? If TRUE, the quantiles of the eigengene correlation matrices (interpreted as a single vectors of non-redundant components) will be equalized across the input data sets. Note that although this seems like a reasonable option, it should be considered experimental and not necessarily recommended.

quantileSummaryForModuleMerging

One of "mean" or "median". If quantile equalization of the module eigengene networks is performed, the resulting "normal" quantiles will be given by this function of the corresponding quantiles across the input data sets.

mergeCutHeight dendrogram cut height for module merging.

mergeConsensusQuantile

consensus quantile for module merging. See mergeCloseModules for details.

numericLabels logical: should the returned modules be labeled by colors (FALSE), or by num-

bers (TRUE)?

nThreads non-negative integer specifying the number of parallel threads to be used by cer-

tain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calcula-

tions will use 2 threads.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

.. Other arguments. At present these can include reproduceBranchEigennodeQuantileError

that instructs the function to reproduce a bug in branch eigennode dissimilarity

calculations for purposes if reproducing old reults.

Details

The function starts by optionally filtering out samples that have too many missing entries and genes that have either too many missing entries or zero variance in at least one set. Genes that are filtered out are left unassigned by the module detection. Returned eigengenes will contain NA in entries corresponding to filtered-out samples.

If blocks is not given and the number of genes exceeds maxBlockSize, genes are pre-clustered into blocks using the function consensusProjectiveKMeans; otherwise all genes are treated in a single block.

For each block of genes, the network is constructed and (if requested) topological overlap is calculated in each set. To minimize memory usage, calculated topological overlaps are optionally saved to disk in chunks until they are needed again for the calculation of the consensus network topological overlap.

Before calculation of the consensus Topological Overlap, individual TOMs are optionally calibrated. Calibration methods include single quantile scaling and full quantile normalization.

Single quantile scaling raises individual TOM in sets 2,3,... to a power such that the quantiles given by calibrationQuantile agree with the quantile in set 1. Since the high TOMs are usually the most important for module identification, the value of calibrationQuantile is close to (but not equal) 1. To speed up quantile calculation, the quantiles can be determined on a randomly-chosen component subset of the TOM matrices.

Full quantile normalization, implemented in normalize.quantiles, adjusts the TOM matrices such that all quantiles equal each other (and equal to the quantiles of the component-wise average of the individual TOM matrices).

Note that network calibration is performed separately in each block, i.e., the normalizing transformation may differ between blocks. This is necessary to avoid manipulating a full TOM in memory.

The consensus TOM is calculated as the component-wise consensusQuantile quantile of the individual (set) TOMs; that is, for each gene pair (TOM entry), the consensusQuantile quantile across all input sets. Alternatively, one can also use (weighted) component-wise mean across all imput data sets. If requested, the consensus topological overlaps are saved to disk for later use.

Genes are then clustered using average linkage hierarchical clustering and modules are identified in the resulting dendrogram by the Dynamic Hybrid tree cut. Found modules are trimmed of genes whose consensus module membership kME (that is, correlation with module eigengene) is less than minKMEtoStay. Modules in which fewer than minCoreKMESize genes have consensus KME higher than minCoreKME are disbanded, i.e., their constituent genes are pronounced unassigned.

After all blocks have been processed, the function checks whether there are genes whose KME in the module they assigned is lower than KME to another module. If p-values of the higher correlations are smaller than those of the native module by the factor reassignThresholdPS (in every set), the gene is re-assigned to the closer module.

In the last step, modules whose eigengenes are highly correlated are merged. This is achieved by clustering module eigengenes using the dissimilarity given by one minus their correlation, cutting the dendrogram at the height mergeCutHeight and merging all modules on each branch. The process is iterated until no modules are merged. See mergeCloseModules for more details on module merging.

The argument quick specifies the precision of handling of missing data in the correlation calculations. Zero will cause all calculations to be executed precisely, which may be significantly slower than calculations without missing data. Progressively higher values will speed up the calculations but introduce progressively larger errors. Without missing data, all column means and variances can be pre-calculated before the covariances are calculated. When missing data are present, exact calculations require the column means and variances to be calculated for each covariance. The approximate calculation uses the pre-calculated mean and variance and simply ignores missing data in the covariance calculation. If the number of missing data is high, the pre-calculated means and variances may be very different from the actual ones, thus potentially introducing large errors. The quick value times the number of rows specifies the maximum difference in the number of missing entries for mean and variance calculations on the one hand and covariance on the other hand that will be tolerated before a recalculation is triggered. The hope is that if only a few missing data are treated approximately, the error introduced will be small but the potential speedup can be significant.

Value

A list with the following components:

colors module assignment of all input genes. A vector containing either character

strings with module colors (if input numericLabels was unset) or numeric module labels (if numericLabels was set to TRUE). The color "grey" and the numeric

label 0 are reserved for unassigned genes.

unmergedColors module colors or numeric labels before the module merging step.

multiMEs module eigengenes corresponding to the modules returned in colors, in multi-

set format. A vector of lists, one per set, containing eigengenes, proportion

of variance explained and other information. See multiSetMEs for a detailed description.

goodSamples a list, with one component per input set. Each component is a logical vector with

one entry per sample from the corresponding set. The entry indicates whether

the sample in the set passed basic quality control criteria.

goodGenes a logical vector with one entry per input gene indicating whether the gene passed

basic quality control criteria in all sets.

dendrograms a list with one component for each block of genes. Each component is the

hierarchical clustering dendrogram obtained by clustering the consensus gene

dissimilarity in the corresponding block.

TOMFiles if saveConsensusTOMs==TRUE, a vector of character strings, one string per block,

giving the file names of files (relative to current directory) in which blockwise

topological overlaps were saved.

blockGenes a list with one component for each block of genes. Each component is a vector

giving the indices (relative to the input multiExpr) of genes in the correspond-

ing block.

blocks if input blocks was given, its copy; otherwise a vector of length equal number

of genes giving the block label for each gene. Note that block labels are not necessarilly sorted in the order in which the blocks were processed (since we do

not require this for the input blocks). See blockOrder below.

blockOrder a vector giving the order in which blocks were processed and in which blockGenes

above is returned. For example, blockOrder[1] contains the label of the first-

processed block.

originCount A vector of length nSets that contains, for each set, the number of (calibrated)

elements that were less than or equal the consensus for that element.

networkCalibrationSamples

if the input getNetworkCalibrationSamples is TRUE, this component is a list with one component per block. Each component is again a list with two components: sampleIndex contains indices of the distance structure in which TOM is stored that were sampled, and TOMSamples is a matrix whose rows correspond to

TOM samples and columns to individual set. Hence, networkCalibrationSamples[[blockNo]]\$TOMSa setNo] contains the TOM entry that corresponds to element networkCalibrationSamples[[blockNo]]

of the TOM distance structure in block blockNo and set setNo. (For details on

the distance structure, see dist.)

Note

If the input datasets have large numbers of genes, consider carefully the maxBlockSize as it significantly affects the memory footprint (and whether the function will fail with a memory allocation error). From a theoretical point of view it is advantageous to use blocks as large as possible; on the other hand, using smaller blocks is substantially faster and often the only way to work with large numbers of genes. As a rough guide, it is unlikely a standard desktop computer with 4GB memory or less will be able to work with blocks larger than 7000 genes.

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

```
goodSamplesGenesMS for basic quality control and filtering;
adjacency, TOMsimilarity for network construction;
hclust for hierarchical clustering;
cutreeDynamic for adaptive branch cutting in hierarchical clustering dendrograms;
mergeCloseModules for merging of close modules.
```

blockwiseIndividualTOMs

Calculation of block-wise topological overlaps

Description

Calculates topological overlaps in the given (expression) data. If the number of variables (columns) in the input data is too large, the data is first split using pre-clustering, then topological overlaps are calculated in each block.

Usage

```
blockwiseIndividualTOMs(
   multiExpr,
   multiWeights = NULL,

# Data checking options

checkMissingData = TRUE,

# Blocking options

blocks = NULL,
   maxBlockSize = 5000,
   blockSizePenaltyPower = 5,
   nPreclusteringCenters = NULL,
   randomSeed = 54321,

# Network construction arguments: correlation options

corType = "pearson",
   maxPOutliers = 1,
   quickCor = 0,
```

```
pearsonFallback = "individual",
cosineCorrelation = FALSE,
# Adjacency function options
power = 6,
networkType = "unsigned",
checkPower = TRUE,
replaceMissingAdjacencies = FALSE,
# Topological overlap options
TOMType = "unsigned",
TOMDenom = "min",
suppressTOMForZeroAdjacencies = FALSE,
suppressNegativeTOM = FALSE,
# Save individual TOMs? If not, they will be returned in the session.
saveTOMs = TRUE,
individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",
# General options
nThreads = 0,
useInternalMatrixAlgebra = FALSE,
verbose = 2, indent = 0)
```

Arguments

multiExpr

expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights

optional observation weights in the same format (and dimensions) as multiExpr. These weights are used in correlation calculation.

checkMissingData

logical: should data be checked for excessive numbers of missing entries in genes and samples, and for genes with zero variance? See details.

blocks

optional specification of blocks in which hierarchical clustering and module detection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the corresponding gene belongs.

maxBlockSize

integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not exceed maxBlockSize.

blockSizePenaltyPower

number specifying how strongly blocks should be penalized for exceeding the

> maximum size. Set to a lrge number or Inf if not exceeding maximum block size is very important.

nPreclusteringCenters

number of centers for pre-clustering. Larger numbers typically results in better

but slower pre-clustering. The default is as.integer(min(nGenes/20, 100*nGenes/preferredSize))

and is an attempt to arrive at a reasonable number given the resources available.

randomSeed integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit. If NULL is given,

the function will not save and restore the seed.

corType character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pariwise.complete.obs

option.

only used for corType=="bicor". Specifies the maximum percentile of data maxPOutliers

that can be considered outliers on either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar

(but not equal to) Pearson correlation.

quickCor real number between 0 and 1 that controls the handling of missing data in the

calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation, if used, should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE). Has no effect for Pearson correlation. See bicor.

cosineCorrelation

logical: should the cosine version of the correlation calculation be used? The cosine calculation differs from the standard one in that it does not subtract the

mean.

soft-thresholding power for network construction. Either a single number or a power

vector of the same length as the number of sets, with one power for each set.

network type. Allowed values are (unique abbreviations of) "unsigned", "signed", networkType

"signed hybrid". See adjacency.

checkPower logical: should basic sanity check be performed on the supplied power? If you

would like to experiment with unusual powers, set the argument to FALSE and

proceed with caution.

replaceMissingAdjacencies

logical: should missing values in calculated adjacency be replaced by 0?

TOMType one of "none", "unsigned", "signed", "signed Nowick", "unsigned 2", "signed

2" and "signed Nowick 2". If "none", adjacency will be used for clustering.

See TOMsimilarityFromExpr for details.

TOMDenom a character string specifying the TOM variant to be used. Recognized values are

"min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results in certain special situations but at this time

should be considered experimental.

suppressTOMForZeroAdjacencies

Logical: should TOM be set to zero for zero adjacencies?

suppressNegativeTOM

Logical: should the result be set to zero when negative? Negative TOM values

can occur when TOMType is "signed Nowick".

saveTOMs logical: should calculated TOMs be saved to disk (TRUE) or returned in the re-

turn value (FALSE)? Returning calculated TOMs via the return value ay be more convenient bt not always feasible if the matrices are too big to fit all in memory

at the same time.

individualTOMFileNames

character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error

will be generated.

nThreads non-negative integer specifying the number of parallel threads to be used by cer-

tain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calcula-

tions will use 2 threads.

useInternalMatrixAlgebra

Logical: should WGCNA's own, slow, matrix multiplication be used instead of

R-wide BLAS? Only useful for debugging.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The function starts by optionally filtering out samples that have too many missing entries and genes that have either too many missing entries or zero variance in at least one set. Genes that are filtered out are excluded from the TOM calculations.

If blocks is not given and the number of genes exceeds maxBlockSize, genes are pre-clustered into blocks using the function consensusProjectiveKMeans; otherwise all genes are treated in a single block.

For each block of genes, the network is constructed and (if requested) topological overlap is calculated in each set. The topological overlaps can be saved to disk as RData files, or returned directly within the return value (see below). Note that the matrices can be big and returning them within the return value can quickly exhaust the system's memory. In particular, if the block-wise calculation is necessary, it is nearly certain that returning all matrices via the return value will be impossible.

Value

A list with the following components:

actualTOMFileNames

Only returned if input saveTOMs is TRUE. A matrix of character strings giving the file names in which each block TOM is saved. Rows correspond to data sets and columns to blocks.

TOMSimilarities

Only returned if input saveTOMs is FALSE. A list in which each component corresponds to one block. Each component is a matrix of dimensions (N times (number of sets)), where N is the length of a distance structure corresponding to the block. That is, if the block contains n genes, N=n*(n-1)/2. Each column of the matrix contains the topological overlap of variables in the corresponding set (and the corresponding block), arranged as a distance structure. Do note however that the topological overlap is a similarity (not a distance).

blocks

if input blocks was given, its copy; otherwise a vector of length equal number of genes giving the block label for each gene. Note that block labels are not necessarilly sorted in the order in which the blocks were processed (since we do not require this for the input blocks). See blockOrder below.

blockGenes

a list with one component for each block of genes. Each component is a vector giving the indices (relative to the input multiExpr) of genes in the corresponding block.

goodSamplesAndGenes

if input checkMissingData is TRUE, the output of the function goodSamplesGenesMS. A list with components goodGenes (logical vector indicating which genes passed the missing data filters), goodSamples (a list of logical vectors indicating which samples passed the missing data filters in each set), and allOK (a logical indicating whether all genes and all samples passed the filters). See goodSamplesGenesMS for more details. If checkMissingData is FALSE, goodSamplesAndGenes contains a list of the same type but indicating that all genes and all samples passed the missing data filters.

The following components are present mostly to streamline the interaction of this function with blockwiseConsensusModules.

nGGenes Number of genes that passed missing data filters (if input checkMissingData is

TRUE), or the number of all genes (if checkMissingData is FALSE).

gBlocks the vector blocks (above), restricted to good genes only.

nThreads number of threads used to calculate correlation and TOM matrices.

saveTOMs logical: were calculated matrices saved in files (TRUE) or returned in the return

value (FALSE)?

```
intNetworkType, intCorType
```

integer codes for network and correlation type.

nSets number of sets in input data.

setNames the names attribute of input multiExpr.

Author(s)

Peter Langfelder

References

For a general discussion of the weighted network formalism, see

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

The blockwise approach is briefly described in the article describing this package,

Langfelder P, Horvath S (2008) "WGCNA: an R package for weighted correlation network analysis". BMC Bioinformatics 2008, 9:559

See Also

blockwiseConsensusModules

blockwiseModules

Automatic network construction and module detection

Description

This function performs automatic network construction and module detection on large expression datasets in a block-wise manner.

Usage

```
blockwiseModules(
    # Input data

datExpr,
weights = NULL,

# Data checking options
checkMissingData = TRUE,

# Options for splitting data into blocks
blocks = NULL,
```

```
maxBlockSize = 5000,
blockSizePenaltyPower = 5,
 nPreclusteringCenters = as.integer(min(ncol(datExpr)/20,
                            100*ncol(datExpr)/maxBlockSize)),
 randomSeed = 54321,
# load TOM from previously saved file?
loadTOM = FALSE,
 # Network construction arguments: correlation options
 corType = "pearson",
maxPOutliers = 1,
 quickCor = 0,
 pearsonFallback = "individual",
 cosineCorrelation = FALSE,
 # Adjacency function options
 power = 6,
 networkType = "unsigned",
 replaceMissingAdjacencies = FALSE,
 # Topological overlap options
 TOMType = "signed",
 TOMDenom = "min",
 suppressTOMForZeroAdjacencies = FALSE,
 suppressNegativeTOM = FALSE,
 # Saving or returning TOM
 getTOMs = NULL,
 saveTOMs = FALSE,
 saveTOMFileBase = "blockwiseTOM",
 # Basic tree cut options
 deepSplit = 2,
 detectCutHeight = 0.995,
minModuleSize = min(20, ncol(datExpr)/2 ),
 # Advanced tree cut options
maxCoreScatter = NULL, minGap = NULL,
maxAbsCoreScatter = NULL, minAbsGap = NULL,
minSplitHeight = NULL, minAbsSplitHeight = NULL,
```

```
useBranchEigennodeDissim = FALSE,
minBranchEigennodeDissim = mergeCutHeight,
stabilityLabels = NULL,
stabilityCriterion = c("Individual fraction", "Common fraction"),
minStabilityDissim = NULL,
pamStage = TRUE, pamRespectsDendro = TRUE,
# Gene reassignment, module trimming, and module "significance" criteria
reassignThreshold = 1e-6,
minCoreKME = 0.5,
minCoreKMESize = minModuleSize/3,
minKMEtoStay = 0.3,
# Module merging options
mergeCutHeight = 0.15,
impute = TRUE,
trapErrors = FALSE,
# Output options
numericLabels = FALSE,
# Options controlling behaviour
nThreads = 0,
useInternalMatrixAlgebra = FALSE,
useCorOptionsThroughout = TRUE,
verbose = 0, indent = 0,
...)
```

Arguments

datExpr Expression data. A matrix (preferred) or data frame in which columns are genes

and rows ar samples. NAs are allowed, but not too many. See checkMissingData

below and details.

weights optional observation weights in the same format (and dimensions) as datExpr.

These weights are used in correlation calculation.

checkMissingData

logical: should data be checked for excessive numbers of missing entries in

genes and samples, and for genes with zero variance? See details.

blocks optional specification of blocks in which hierarchical clustering and module de-

tection should be performed. If given, must be a numeric vector with one entry

> per column (gene) of exprData giving the number of the block to which the corresponding gene belongs.

maxBlockSize

integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not exceed maxBlockSize.

blockSizePenaltyPower

number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block size is very important.

nPreclusteringCenters

number of centers for pre-clustering. Larger numbers typically results in better but slower pre-clustering.

randomSeed integer to be used as seed for the random number generator before the function starts. If a current seed exists, it is saved and restored upon exit. If NULL is given,

the function will not save and restore the seed.

logical: should Topological Overlap Matrices be loaded from previously saved files (TRUE) or calculated (FALSE)? It may be useful to load previously saved TOM matrices if these have been calculated previously, since TOM calculation is often the most computationally expensive part of network construction and module identification. See saveTOMs and saveTOMFileBase below for when and how TOM files are saved, and what the file names are. If loadTOM is TRUE but the files cannot be found, or do not contain the correct TOM data, TOM will

be recalculated.

character string specifying the correlation to be used. Allowed values are (unique abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pairwise.complete.obs

option.

only used for corType=="bicor". Specifies the maximum percentile of data maxPOutliers

that can be considered outliers on either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar

(but not equal to) Pearson correlation.

real number between 0 and 1 that controls the handling of missing data in the

calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation, if used, should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE). Has no effect for Pearson correlation. See bicor.

loadTOM

corType

quickCor

cosineCorrelation

logical: should the cosine version of the correlation calculation be used? The cosine calculation differs from the standard one in that it does not subtract the

mean.

power soft-thresholding power for network construction.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

replaceMissingAdjacencies

logical: should missing values in the calculation of adjacency be replaced by 0?

TOMType one of "none", "unsigned", "signed", "signed Nowick", "unsigned 2", "signed

2" and "signed Nowick 2". If "none", adjacency will be used for clustering.

See TOMsimilarityFromExpr for details.

TOMDenom a character string specifying the TOM variant to be used. Recognized values

are "min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results but at this time should be considered

experimental.

suppressTOMForZeroAdjacencies

Logical: should TOM be set to zero for zero adjacencies?

suppressNegativeTOM

Logical: should the result be set to zero when negative? Negative TOM values

can occur when TOMType is "signed Nowick".

getTOMs deprecated, please use saveTOMs below.

saveTOMs logical: should the consensus topological overlap matrices for each block be

saved and returned?

saveTOMFileBase

character string containing the file name base for files containing the consensus topological overlaps. The full file names have "block.1.RData", "block.2.RData" etc. appended. These files are standard R data files and can be loaded using the

load function.

deepSplit integer value between 0 and 4. Provides a simplified control over how sensitive

module detection should be to module splitting, with 0 least and 4 most sensitive.

See cutreeDynamic for more details.

detectCutHeight

dendrogram cut height for module detection. See cutreeDynamic for more de-

tails.

minModuleSize minimum module size for module detection. See cutreeDynamic for more de-

tails.

maxCoreScatter maximum scatter of the core for a branch to be a cluster, given as the fraction of

cutHeight relative to the 5th percentile of joining heights. See cutreeDynamic

for more details.

minGap minimum cluster gap given as the fraction of the difference between cutHeight

and the 5th percentile of joining heights. See cutreeDynamic for more details.

maxAbsCoreScatter

maximum scatter of the core for a branch to be a cluster given as absolute heights. If given, overrides maxCoreScatter. See cutreeDynamic for more details.

minAbsGap

minimum cluster gap given as absolute height difference. If given, overrides minGap. See cutreeDynamic for more details.

minSplitHeight

Minimum split height given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. Branches merging below this height will automatically be merged. Defaults to zero but is used only if minAbsSplitHeight below is NULL.

minAbsSplitHeight

Minimum split height given as an absolute height. Branches merging below this height will automatically be merged. If not given (default), will be determined from minSplitHeight above.

useBranchEigennodeDissim

Logical: should branch eigennode (eigengene) dissimilarity be considered when merging branches in Dynamic Tree Cut?

minBranchEigennodeDissim

Minimum consensus branch eigennode (eigengene) dissimilarity for branches to be considered separate. The branch eigennode dissimilarity in individual sets is simly 1-correlation of the eigennodes; the consensus is defined as quantile with probability consensusQuantile.

stabilityLabels

Optional matrix of cluster labels that are to be used for calculating branch dissimilarity based on split stability. The number of rows must equal the number of genes in multiExpr; the number of columns (clusterings) is arbitrary. See branchSplitFromStabilityLabels for details.

stabilityCriterion

One of c("Individual fraction", "Common fraction"), indicating which method for assessing stability similarity of two branches should be used. We recommend "Individual fraction" which appears to perform better; the "Common fraction" method is provided for backward compatibility since it was the (only) method available prior to WGCNA version 1.60.

minStabilityDissim

Minimum stability dissimilarity criterion for two branches to be considered separate. Should be a number between 0 (essentially no dissimilarity required) and 1 (perfect dissimilarity or distinguishability based on stabilityLabels). See branchSplitFromStabilityLabels for details.

pamStage

logical. If TRUE, the second (PAM-like) stage of module detection will be performed. See cutreeDynamic for more details.

pamRespectsDendro

Logical, only used when pamStage is TRUE. If TRUE, the PAM stage will respect the dendrogram in the sense an object can be PAM-assigned only to clusters that lie below it on the branch that the object is merged into. See cutreeDynamic for more details.

minCoreKME

a number between 0 and 1. If a detected module does not have at least minModuleKMESize genes with eigengene connectivity at least minCoreKME, the module is disbanded

(its genes are unlabeled and returned to the pool of genes waiting for mofule detection).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose eigengene connectivity to their module eigengene is lower than

minKMEtoStay are removed from the module.

reassignThreshold

p-value ratio threshold for reassigning genes between modules. See Details.

mergeCutHeight dendrogram cut height for module merging.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

numericLabels logical: should the returned modules be labeled by colors (FALSE), or by num-

bers (TRUE)?

nThreads non-negative integer specifying the number of parallel threads to be used by cer-

tain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calcula-

tions will use 2 threads.

useInternalMatrixAlgebra

Logical: should WGCNA's own, slow, matrix multiplication be used instead of

R-wide BLAS? Only useful for debugging.

useCorOptionsThroughout

Logical: should correlation options passed to network analysis also be used in

calculation of kME? Set to FALSE to reproduce results obtained with WGCNA

1.62 and older.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

... Other arguments.

Details

Before module detection starts, genes and samples are optionally checked for the presence of NAs. Genes and/or samples that have too many NAs are flagged as bad and removed from the analysis; bad genes will be automatically labeled as unassigned, while the returned eigengenes will have NA entries for all bad samples.

If blocks is not given and the number of genes exceeds maxBlockSize, genes are pre-clustered into blocks using the function projectiveKMeans; otherwise all genes are treated in a single block.

For each block of genes, the network is constructed and (if requested) topological overlap is calculated. If requested, the topological overlaps are returned as part of the return value list. Genes are then clustered using average linkage hierarchical clustering and modules are identified in the resulting dendrogram by the Dynamic Hybrid tree cut. Found modules are trimmed of genes whose correlation with module eigengene (KME) is less than minKMEtoStay. Modules in which fewer

than minCoreKMESize genes have KME higher than minCoreKME are disbanded, i.e., their constituent genes are pronounced unassigned.

After all blocks have been processed, the function checks whether there are genes whose KME in the module they assigned is lower than KME to another module. If p-values of the higher correlations are smaller than those of the native module by the factor reassignThresholdPS, the gene is reassigned to the closer module.

In the last step, modules whose eigengenes are highly correlated are merged. This is achieved by clustering module eigengenes using the dissimilarity given by one minus their correlation, cutting the dendrogram at the height mergeCutHeight and merging all modules on each branch. The process is iterated until no modules are merged. See mergeCloseModules for more details on module merging.

The argument quick specifies the precision of handling of missing data in the correlation calculations. Zero will cause all calculations to be executed precisely, which may be significantly slower than calculations without missing data. Progressively higher values will speed up the calculations but introduce progressively larger errors. Without missing data, all column means and variances can be pre-calculated before the covariances are calculated. When missing data are present, exact calculations require the column means and variances to be calculated for each covariance. The approximate calculation uses the pre-calculated mean and variance and simply ignores missing data in the covariance calculation. If the number of missing data is high, the pre-calculated means and variances may be very different from the actual ones, thus potentially introducing large errors. The quick value times the number of rows specifies the maximum difference in the number of missing entries for mean and variance calculations on the one hand and covariance on the other hand that will be tolerated before a recalculation is triggered. The hope is that if only a few missing data are treated approximately, the error introduced will be small but the potential speedup can be significant.

Value

blockGenes

A list with the following components:

colors	a vector of color or numeric module labels for all genes.
unmergedColors	a vector of color or numeric module labels for all genes before module merging.
MEs	a data frame containing module eigengenes of the found modules (given by colors).
goodSamples	numeric vector giving indices of good samples, that is samples that do not have too many missing entries.
goodGenes	numeric vector giving indices of good genes, that is genes that do not have too many missing entries.
dendrograms	a list whose components conatain hierarchical clustering dendrograms of genes in each block.
TOMFiles	if saveTOMs==TRUE, a vector of character strings, one string per block, giving the file names of files (relative to current directory) in which blockwise topological overlaps were saved.

a list whose components give the indices of genes in each block.

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blocks if input blocks was given, its copy; otherwise a vector of length equal number

of genes giving the block label for each gene. Note that block labels are not necessarilly sorted in the order in which the blocks were processed (since we do

not require this for the input blocks). See blockOrder below.

blockOrder a vector giving the order in which blocks were processed and in which blockGenes

above is returned. For example, blockOrder[1] contains the label of the first-

processed block.

MESOK logical indicating whether the module eigengenes were calculated without er-

rors.

Note

significantly affects the memory footprint (and whether the function will fail with a memory allocation error). From a theoretical point of view it is advantageous to use blocks as large as possible; on the other hand, using smaller blocks is substantially faster and often the only way to work with large numbers of genes. As a rough guide, it is unlikely a standard desktop computer with 4GB memory or less will be able to work with blocks larger than 8000 genes.

Author(s)

Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

goodSamplesGenes for basic quality control and filtering;
adjacency, TOMsimilarity for network construction;
hclust for hierarchical clustering;
cutreeDynamic for adaptive branch cutting in hierarchical clustering dendrograms;

mergeCloseModules for merging of close modules.

BloodLists Blood Cell Types with Corresponding Gene Markers

Description

This matrix gives a predefined set of marker genes for many blood cell types, as reported in several previously-published studies. It is used with userListEnrichment to search user-defined gene lists for enrichment.

64 blueWhiteRed

Usage

```
data(BloodLists)
```

Format

A 2048 x 2 matrix of characters containing Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <Blood cell type>__<reference>, where the references can be found at userListEnrichment. Note that the matrix is sorted first by Category and then by Gene, such that all genes related to the same category are listed sequentially.

Source

For references used in this variable, please see userListEnrichment

Examples

```
data(BloodLists)
head(BloodLists)
```

blueWhiteRed

Blue-white-red color sequence

Description

Generate a blue-white-red color sequence of a given length.

Usage

Arguments

n number of colors to be returned.

gamma color change power.

endSaturation a number between 0 and 1 giving the saturation of the colors that will represent

the ends of the scale. Lower numbers mean less saturation (lighter colors).

blueEnd vector of length 3 giving the RGB relative values (between 0 and 1) for the blue

or negative end color.

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redEnd vector of length 3 giving the RGB relative values (between 0 and 1) for the red

or positive end color.

middle vector of length 3 giving the RGB relative values (between 0 and 1) for the

middle of the scale.

Details

The function returns a color vector that starts with blue, gradually turns into white and then to red. The power gamma can be used to control the behaviour of the quarter- and three quarter-values (between blue and white, and white and red, respectively). Higher powers will make the mid-colors more white, while lower powers will make the colors more saturated, respectively.

Value

A vector of colors of length n.

Author(s)

Peter Langfelder

See Also

numbers2colors for a function that produces a color representation for continuous numbers.

Examples

```
par(mfrow = c(3, 1))
displayColors(blueWhiteRed(50));
title("gamma = 1")
displayColors(blueWhiteRed(50, 3));
title("gamma = 3")
displayColors(blueWhiteRed(50, 0.5));
title("gamma = 0.5")
```

BrainLists

Brain-Related Categories with Corresponding Gene Markers

Description

This matrix gives a predefined set of marker genes for many brain-related categories (ie., cell type, organelle, changes with disease, etc.), as reported in several previously-published studies. It is used with userListEnrichment to search user-defined gene lists for enrichment.

Usage

```
data(BrainLists)
```

66 BrainRegionMarkers

Format

A 48319 x 2 matrix of characters containing Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <Brain descriptor>__<reference>, where the references can be found at userListEnrichment. Note that the matrix is sorted first by Category and then by Gene, such that all genes related to the same category are listed sequentially.

Source

For references used in this variable, please see userListEnrichment

Examples

```
data(BrainLists)
head(BrainLists)
```

BrainRegionMarkers

Gene Markers for Regions of the Human Brain

Description

This matrix gives a predefined set of marker genes for many regions of the human brain, using data from the Allen Human Brain Atlas (https://human.brain-map.org/) as reported in: Hawrylycz MJ, Lein ES, Guillozet-Bongaarts AL, Shen EH, Ng L, Miller JA, et al. (2012) An Anatomically Comprehensive Atlas of the Adult Human Brain Transcriptome. Nature (in press). It is used with userListEnrichment to search user-defined gene lists for enrichment.

Usage

```
data(BrainRegionMarkers)
```

Format

A 28477 x 2 matrix of characters containing Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <Brain Region>_<Marker Type>__HBA. Note that the matrix is sorted first by Category and then by Gene, such that all genes related to the same category are listed sequentially.

Source

For references used in this variable, or other information, please see userListEnrichment

Examples

```
data(BrainRegionMarkers)
head(BrainRegionMarkers)
```

branchEigengeneDissim Branch dissimilarity based on eigennodes (eigengenes).

Description

Calculation of branch dissimilarity based on eigennodes (eigengenes) in single set and multi-data situations. This function is used as a plugin for the dynamicTreeCut package and the user should not call this function directly. This function is experimental and subject to change.

Usage

```
branchEigengeneDissim(
  expr,
  branch1, branch2,
  corFnc = cor, corOptions = list(use = "p"),
  signed = TRUE, ...)
branchEigengeneSimilarity(
  expr,
  branch1,
 branch2,
  networkOptions,
  returnDissim = TRUE, ...)
mtd.branchEigengeneDissim(
 multiExpr,
 branch1, branch2,
  corFnc = cor, corOptions = list(use = 'p'),
  consensusQuantile = 0,
  signed = TRUE, reproduceQuantileError = FALSE, ...)
hierarchicalBranchEigengeneDissim(
    multiExpr,
    branch1, branch2,
    networkOptions,
    consensusTree, ...)
```

Arguments

expr Expression data.

multiExpr Expression data in multi-set format.

branch1 Branch 1. branch2 Branch 2.

corFnc Correlation function.

corOptions Other arguments to the correlation function.

consensusQuantile

Consensus quantile.

signed Should the network be considered signed?

reproduceQuantileError

Logical: should an error in the calculation from previous versions, which caused

the true consensus quantile to be 1-consensusQuantile rather than consensusQuantile,

be reproduced? Use this only to reproduce old calculations.

networkOptions An object of class NetworkOptions giving the network construction options to

be used in the calculation of the similarity.

returnDissim Logical: if TRUE, dissimarity, rather than similarity, will be returned.

consensusTree A list of class ConsensusTree specifying the consensus calculation. Note that

calibration options within the consensus specifications are ignored: since the consensus is calulated from entries representing a single value, calibration would

not make sense.

... Other arguments for compatibility; currently unused.

Details

These functions calculate the similarity or dissimilarity of two groups of genes (variables) in expr or multiExpr using correlations of the first singular vectors ("eigengenes"). For a single data set (branchEigengeneDissim and branchEigengeneSimilarity), the similarity is the correlation, and dissimilarity 1-correlation of the first signular vectors.

Functions mtd.branchEigengeneDissim and hierarchicalBranchEigengeneDissim calculate consensus eigengene dissimilarity. Function mtd.branchEigengeneDissim calculates a simple ("flat") consensus of branch eigengene similarities across the given data set, at the given consensus quantile. Function hierarchicalBranchEigengeneDissim can calculate a hierarchical consensus in which consensus calculations are hierarchically nested.

Value

A single number, the dissimilarity for branchEigengeneDissim, mtd.branchEigengeneDissim, and hierarchicalBranchEigengeneDissim.

branchEigengeneSimilarity returns similarity or dissimilarity, depending on imput.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusCalculation

branchSplit 69

lit Branch split.

Description

Calculation of branch split based on expression data. This function is used as a plugin for the dynamicTreeCut package and the user should not call this function directly.

Usage

```
branchSplit(
  expr,
  branch1, branch2,
  discardProp = 0.05, minCentralProp = 0.75,
  nConsideredPCs = 3,
  signed = FALSE,
  getDetails = TRUE, ...)
```

Arguments

expr	Expression data.
branch1	Branch 1,
branch2	Branch 2.
discardProp	Proportion of data to be discarded as outliers.
minCentralProp	Minimum central proportion
nConsideredPCs	Number of principal components to consider.
signed	Should the network be considered signed?
getDetails	Should details of the calculation be returned?
	Other arguments. Present for compatibility; currently unusued.

Value

A single number or a list containing detils of the calculation.

Author(s)

Peter Langfelder

70 branchSplit.dissim

branchSplit.dissim Branch split based on dissimilarity.

Description

Calculation of branch split based on a dissimilarity matrix. This function is used as a plugin for the dynamicTreeCut package and the user should not call this function directly. This function is experimental and subject to change.

Usage

```
branchSplit.dissim(
  dissimMat,
  branch1, branch2,
  upperP,
  minNumberInSplit = 5,
  getDetails = FALSE, ...)
```

Arguments

dissimMat Dissimilarity matrix.

branch1 Branch 1.
branch2 Branch 2.

upperP Percentile of (closest) objects to be considered.

minNumberInSplit

Minimum number of objects to be considered.

getDetails Should details of the calculation be returned?

... Other arguments for compatibility; currently unused.

Value

A single number or a list containing details of the calculation.

Author(s)

Peter Langfelder

```
branchSplitFromStabilityLabels
```

Branch split (dissimilarity) statistics derived from labels determined from a stability study

Description

These functions evaluate how different two branches are based on a series of cluster labels that are usually obtained in a stability study but can in principle be arbitrary. The idea is to quantify how well membership on the two tested branches can be predicted from clusters in the given stability labels.

Usage

Arguments

branch1 A vector of indices giving members of branch 1. branch2 A vector of indices giving members of branch 1. stabilityLabels A matrix of cluster labels. Each column corresponds to one clustering and each row to one object (whose indices branch1 and branch2 refer to). Label or labels that do not constitute proper clusters in stabilityLabels, for ignoreLabels example because they label unassigned objects. verbose integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose. indent indentation for diagnostic messages. Zero means no indentation, each unit adds two spaces. Ignored.

Details

The idea is to measure how well clusters in stabilityLabels can distinguish the two given branches. For example, if a cluster C intersects with branch1 but not branch2, it can distinguish branches 1 and 2 perfectly. On the other hand, if there is a cluster C that contains both branch 1 and branch 2, the two branches are indistinguishable (based on the test clustering). The three functions differ in the details of the similarity calculation.

branchSplitFromStabilityLabels.individualFraction: Currently the recommended branch split calculation method, and default for hierarchicalConsensusModules. For each branch and all clusters that overlap with the branch (not necessarily with the other branch), calculate the fraction of the cluster objects (restricted to the two branches) that belongs to the branch. For each branch, sum these fractions over all clusters. If this number is relatively low, around 0.5, it means most elements are in non-discriminative clusters.

branchSplitFromStabilityLabels: This was the original branch split measure and for backward compatibility it still is the default method in blockwiseModules and blockwiseConsensusModules. For each cluster C in each clustering in stabilityLabels, its contribution to the branch similarity is min(r1, r2), where r1 = lintersect(C, branch1)l/lbranch1l and r2 = lintersect(C, branch2)l/lbranch2l. The statistics for clusters in each clustering are added; the sums are then averaged across the clusterings.

branchSplitFromStabilityLabels.prediction: Use only for experiments, not recommended for actual analyses because it is not stable under small changes in the branch membership. For each cluster that overlaps with both branches, count the objects in the branch with which the cluster has a smaller overlap and add it to the score for that branch. The final counts divided by number of genes on branch give a "indistinctness" score; take the larger of the two indistinctness scores and call this the similarity.

Since the result of the last two calculations is a similarity statistic, the final dissimilarity is defined as 1-similarity. The dissimilarity ranges between 0 (branch1 and branch2 are indistinguishable) and 1 (branch1 and branch2 are perfectly distinguishable).

These statistics are quite simple and do not correct for similarity that would be expected by chance. On the other hand, all 3 statistics are fairly (though not perfectly) stable under splitting and joining of clusters in stabilityLabels.

Value

Branch dissimilarity (a single number between 0 and 1).

Author(s)

Peter Langfelder

See Also

These function are utilized in blockwiseModules, blockwiseConsensusModules and hierarchicalConsensusModules.

checkAdjMat 73

checkAdjMat	Check adjacency matrix	

Description

Checks a given matrix for properties that an adjacency matrix must satisfy.

Usage

```
checkAdjMat(adjMat, min = 0, max = 1)
checkSimilarity(similarity, min = -1, max = 1)
```

Arguments

adjMat matrix to be checked
similarity matrix to be checked
min minimum allowed value for entries of the input
max maximum allowed value for entries of the input

Details

The function checks whether the given matrix really is a 2-dimensional numeric matrix, whether it is square, symmetric, and all finite entries are between min and max. If any of the conditions is not met, the function issues an error.

Value

None. The function returns normally if all conditions are met.

Author(s)

Peter Langfelder

See Also

adjacency

74 checkSets

	checkSets	Check structure and retrieve sizes of a group of datasets.
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Description

Checks whether given sets have the correct format and retrieves dimensions.

Usage

```
checkSets(data, checkStructure = FALSE, useSets = NULL)
```

Arguments

data A vector of lists; in each list there must be a component named data whose

content is a matrix or dataframe or array of dimension 2.

checkStructure If FALSE, incorrect structure of data will trigger an error. If TRUE, an appropriate

flag (see output) will be set to indicate whether data has correct structure.

useSets Optional specification of entries of the vector data that are to be checked. De-

faults to all components. This may be useful when data only contains informa-

tion for some of the sets.

Details

For multiset calculations, many quantities (such as expression data, traits, module eigengenes etc) are presented by a common structure, a vector of lists (one list for each set) where each list has a component data that contains the actual (expression, trait, eigengene) data for the corresponding set in the form of a dataframe. This funtion checks whether data conforms to this convention and retrieves some basic dimension information (see output).

Value

A list with components

nSets Number of sets (length of the vector data).

nGenes Number of columns in the data components in the lists. This number must be

the same for all sets.

nSamples A vector of length nSets giving the number of rows in the data components.

structureOK Only set if the argument checkStructure equals TRUE. The value is TRUE if

the paramter data passes a few tests of its structure, and FALSE otherwise. The tests are not exhaustive and are meant to catch obvious user errors rather than be

bulletproof.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

chooseOneHubInEachModule

Chooses a single hub gene in each module

Description

chooseOneHubInEachModule returns one gene in each module with high connectivity, given a number of randomly selected genes to test.

Usage

```
chooseOneHubInEachModule(
   datExpr,
   colorh,
   numGenes = 100,
   omitColors = "grey",
   power = 2,
   type = "signed",
   ...)
```

Arguments

datExpr	Gene expression data with rows as samples and columns as genes.
colorh	The module assignments (color vectors) corresponding to the columns in dat- Expr.
numGenes	Th number of random genes to select per module. Higher number of genes increases the accuracy of hub selection but slows down the function.
omitColors	All colors in this character vector (default is "grey") are ignored by this function.
power	Power to use for the adjacency network (default = 2).
type	What type of network is being entered. Common choices are "signed" (default) and "unsigned". With "signed" negative correlations count against, whereas with "unsigned" negative correlations are treated identically as positive correlations.
	Any other parameters accepted by the *adjacency* function

Value

Both functions output a character vector of genes, where the genes are the hub gene picked for each module, and the names correspond to the module in which each gene is a hub.

Author(s)

Jeremy Miller

Examples

```
## Example: first simulate some data.
MEturquoise = sample(1:100,50)
MEblue = sample(1:100,50)
MEbrown = sample(1:100,50)
MEyellow = sample(1:100,50)
          = c(MEyellow[1:30], sample(1:100,20))
MEgreen
         = c(MEbrown [1:20], sample(1:100,30))
MEblack
           = c(MEblue [1:25], sample(1:100,25))
      = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen, MEred, MEblack)
dat1 = simulateDatExpr(ME,300,c(0.2,0.1,0.08,0.051,0.05,0.042,0.041,0.3),
                        signed=TRUE)
      = TOMsimilarityFromExpr(dat1$datExpr, networkType="signed")
colnames(TOM1) <- rownames(TOM1) <- colnames(dat1$datExpr)</pre>
tree1 <- tree2 <- fastcluster::hclust(as.dist(1-TOM1),method="average")</pre>
colorh = labels2colors(dat1$allLabels)
        = chooseOneHubInEachModule(dat1$datExpr, colorh)
hubs
hubs
```

chooseTopHubInEachModule

Chooses the top hub gene in each module

Description

chooseTopHubInEachModule returns the gene in each module with the highest connectivity, looking at all genes in the expression file.

Usage

```
chooseTopHubInEachModule(
   datExpr,
   colorh,
   omitColors = "grey",
   power = 2,
   type = "signed",
   ...)
```

Arguments

datExpr Gene expression data with rows as samples and columns as genes.

The module assignments (color vectors) corresponding to the columns in datExpr.

Mall colors in this character vector (default is "grey") are ignored by this function.

Power bower ouse for the adjacency network (default = 2).

clusterCoef 77

type What type of network is being entered. Common choices are "signed" (default) and "unsigned". With "signed" negative correlations count against, whereas with "unsigned" negative correlations are treated identically as positive correlations.

... Any other parameters accepted by the *adjacency* function

Value

Both functions output a character vector of genes, where the genes are the hub gene picked for each module, and the names correspond to the module in which each gene is a hub.

Author(s)

Jeremy Miller

Examples

```
## Example: first simulate some data.
MEturquoise = sample(1:100,50)
MEblue
           = sample(1:100,50)
MEbrown
           = sample(1:100,50)
MEyellow
           = sample(1:100,50)
           = c(MEyellow[1:30], sample(1:100,20))
MEgreen
         = c(MEbrown [1:20], sample(1:100,30))
MEred
MEblack
            = c(MEblue [1:25], sample(1:100,25))
       = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen, MEred, MEblack)
dat1 = simulateDatExpr(ME,300,c(0.2,0.1,0.08,0.051,0.05,0.042,0.041,0.3), signed=TRUE)
colorh = labels2colors(dat1$allLabels)
        = chooseTopHubInEachModule(dat1$datExpr, colorh)
hubs
hubs
```

clusterCoef

Clustering coefficient calculation

Description

This function calculates the clustering coefficients for all nodes in the network given by the input adjacency matrix.

Usage

```
clusterCoef(adjMat)
```

Arguments

adjMat adjacency matrix

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Value

A vector of clustering coefficients for each node.

Author(s)

Steve Horvath

coClustering

Co-clustering measure of cluster preservation between two clusterings

Description

The function calculates the co-clustering statistics for each module in the reference clustering.

Usage

```
coClustering(clusters.ref, clusters.test, tupletSize = 2, unassignedLabel = 0)
```

Arguments

clusters.ref Reference input clustering. A vector in which each element gives the cluster

label of an object.

clusters.test Test input clustering. Must be a vector of the same size as cluster.ref.

tupletSize Co-clutering tuplet size.

unassignedLabel

Optional specification of a clustering label that denotes unassigned objects. Objects with this label are excluded from the calculation.

Details

Co-clustering of cluster q in the reference clustering and cluster q' in the test clustering measures the overlap of clusters q and q' by the number of tuplets that can be chosen from the overlap of clusters q and q' relative to the number of tuplets in cluster q. To arrive at a co-clustering measure for cluster q, we sum the co-clustering of q and q' over all clusters q' in the test clustering. A value close to 1 indicates high preservation of the reference cluster in the test clustering, while a value close to zero indicates a low preservation.

Value

A vector in which each component corresponds to a cluster in the reference clustering. Entries give the co-clustering measure of cluster preservation.

Author(s)

Peter Langfelder

References

For example, see Langfelder P, Luo R, Oldham MC, Horvath S (2011) Is My Network Module Preserved and Reproducible? PLoS Comput Biol 7(1): e1001057. Co-clustering is discussed in the Methods Supplement (Supplementary text 1) of that article.

See Also

modulePreservation for a large suite of module preservation statistics coClustering.permutationTest for a permutation test for co-clustering significance

Examples

```
# An example with random (unrelated) clusters:
set.seed(1);
nModules = 10;
nGenes = 1000;
cl1 = sample(c(1:nModules), nGenes, replace = TRUE);
cl2 = sample(c(1:nModules), nGenes, replace = TRUE);
coClustering(cl1, cl2)
# For the same reference and test clustering:
coClustering(cl1, cl1)
```

coClustering.permutationTest

Permutation test for co-clustering

Description

This function calculates permutation Z statistics that measure how different the co-clustering of modules in a reference and test clusterings is from random.

Usage

```
coClustering.permutationTest(
    clusters.ref, clusters.test,
    tupletSize = 2,
    nPermutations = 100,
    unassignedLabel = 0,
    randomSeed = 12345, verbose = 0, indent = 0)
```

Arguments

clusters.ref Reference input clustering. A vector in which each element gives the cluster

label of an object.

clusters.test Test input clustering. Must be a vector of the same size as cluster.ref.

tupletSize Co-clutering tuplet size.

nPermutations Number of permutations to execute. Since the function calculates parametric

p-values, a relatively small number of permutations (at least 50) should be suf-

ficient.

unassignedLabel

Optional specification of a clustering label that denotes unassigned objects. Ob-

jects with this label are excluded from the calculation.

randomSeed Random seed for initializing the random number generator. If NULL, the gener-

ator is not initialized (useful for calling the function sequentially). The default

assures reproducibility.

verbose If non-zero, function will print out progress messages.

indent Indentation for progress messages. Each unit adds two spaces.

Details

This function performs a permutation test to determine whether observed co-clustering statistics are significantly different from those expected by chance. It returns the observed co-clustering as well as the permutation Z statistic, calculated as (observed – mean)/sd, where mean and standard deviation of the co-clustering when the test clustering is repeatedly randomly permuted.

Value

observed the observed co-clustering measures for clusters in clusters.ref

Z permutation Z statics

permuted.mean means of the co-clustering measures when the test clustering is permuted

permuted.sd standard deviations of the co-clustering measures when the test clustering is

permuted

permuted.cc values of the co-clustering measure for each permutation of the test clustering. A

matrix of dimensions (number of permutations)x(number of clusters in reference

clustering).

Author(s)

Peter Langfelder

References

For example, see Langfelder P, Luo R, Oldham MC, Horvath S (2011) Is My Network Module Preserved and Reproducible? PLoS Comput Biol 7(1): e1001057. Co-clustering is discussed in the Methods Supplement (Supplementary text 1) of that article.

See Also

coClustering for calculation of the "observed" co-clustering measure modulePreservation for a large suite of module preservation statistics

Examples

```
set.seed(1);
nModules = 5;
nGenes = 100;
cl1 = sample(c(1:nModules), nGenes, replace = TRUE);
cl2 = sample(c(1:nModules), nGenes, replace = TRUE);
cc = coClustering(cl1, cl2)
# Choose a low number of permutations to make the example fast
ccPerm = coClustering.permutationTest(cl1, cl2, nPermutations = 20, verbose = 1);
ccPerm$observed
ccPerm$Z
# Combine cl1 and cl2 to obtain clustering that is somewhat similar to cl1:
c13 = c12;
from1 = sample(c(TRUE, FALSE), nGenes, replace = TRUE);
cl3[from1] = cl1[from1];
ccPerm = coClustering.permutationTest(cl1, cl3, nPermutations = 20, verbose = 1);
# observed co-clustering is higher than before:
ccPerm$observed
# Note the high preservation Z statistics:
ccPerm$Z
```

collapseRows

Select one representative row per group

Description

Abstractly speaking, the function allows one to collapse the rows of a numeric matrix, e.g. by forming an average or selecting one representative row for each group of rows specified by a grouping variable (referred to as rowGroup). The word "collapse" reflects the fact that the method yields a new matrix whose rows correspond to other rows of the original input data. The function implements several network-based and biostatistical methods for finding a representative row for each group specified in rowGroup. Optionally, the function identifies the representative row according to the least number of missing data, the highest sample mean, the highest sample variance, the highest connectivity. One of the advantages of this function is that it implements default settings which have worked well in numerous applications. Below, we describe these default settings in more detail.

Usage

Arguments

datET

matrix or data frame containing numeric values where rows correspond to variables (e.g. microarray probes) and columns correspond to observations (e.g. microarrays). Each row of datET must have a unique row identifier (specified in the vector rowID). The group label of each row is encoded in the vector rowGroup. While rowID should have non-missing, unique values (identifiers), the values of the vector rowGroup will typically not be unique since the function aims to pick a representative row for each group.

rowGroup

character vector whose components contain the group label (e.g. a character string) for each row of datET. This vector needs to have the same length as the vector rowID. In gene expression applications, this vector could contain the gene symbol (or a co-expression module label).

rowID

character vector of row identifiers. This should include all the rows from row-names(datET), but can include other rows. Its entries should be unique (no duplicates) and no missing values are permitted. If the row identifier is missing for a given row, we suggest you remove this row from datET before applying the function.

method

character string for determining which method is used to choose a probe among exactly 2 corresponding rows or when connectivityBasedCollapsing=FALSE. These are the options: "MaxMean" (default) or "MinMean" = choose the row with the highest or lowest mean value, respectively. "maxRowVariance" = choose the row with the highest variance (across the columns of datET). "absMaxMean" or "absMinMean" = choose the row with the highest or lowest mean absolute value. "ME" = choose the eigenrow (first principal component of the rows in each group). Note that with this method option, connectivityBasedCollapsing is automatically set to FALSE. "Average" = for each column, take the average value of the rows in each group "function" = use this method for a userinput function (see the description of the argument "methodFunction"). Note: if method="ME", "Average" or "function", the output parameters "group2row" and "selectedRow" are not informative.

connectivityBasedCollapsing

logical value. If TRUE, groups with 3 or more corresponding rows will be represented by the row with the highest connectivity according to a signed weighted correlation network adjacency matrix among the corresponding rows. Recall that the connectivity is defined as the rows sum of the adjacency matrix. The signed weighted adjacency matrix is defined as A=(0.5+0.5*COR)^power where power is determined by the argument connectivityPower and COR denotes the matrix of pairwise Pearson correlation coefficients among the corresponding rows.

methodFunction character string. It only needs to be specified if method="function" otherwise its input is ignored. Must be a function that takes a Nr x Nc matrix of numbers as input and outputs a vector with the length Nc (e.g., colMeans). This will then be the method used for collapsing values for multiple rows into a single value for the row.

connectivityPower

Positive number (typically integer) for specifying the threshold (power) used to construct the signed weighted adjacency matrix, see the description of connectivityBasedCollapsing. This option is only used if connectivityBasedCollapsing=TRUE.

selectFewestMissing

logical values. If TRUE (default), the input expression matrix is trimmed such that for each group only the rows with the fewest number of missing values are retained. In situations where an equal number of values are missing (or where there is no missing data), all rows for a given group are retained. Whether this value is set to TRUE or FALSE, all rows with >90% missing data are omitted from the analysis.

thresholdCombine

Number between -1 and 1, or NA. If NA (default), this input is ignored. If a number between -1 and 1 is input, this value is taken as a threshold value, and collapseRows proceeds following the "maxMean" method, but ONLY for ids with correlations of R>thresholdCombine. Specifically: ...1) If there is one id/group, keep the id ...2) If there are 2 ids/group, take the maximum mean expression if their correlation is > thresholdCombine ...3) If there are 3+ ids/group, iteratively repeat (2) for the 2 ids with the highest correlation until all ids remaining have correlation < thresholdCombine for each group Note that this option usually results in more than one id per group; therefore, one must use care when implementing this option for use in comparisons between multiple matrices / data frames.

Details

The function is robust to missing data. Also, if rowIDs are missing, they are inferred according to the rownames of datET when possible. When a group corresponds to only 1 row then it is represented by this row since there is no other choice. Having said this, the row may be removed if it contains an excessive amount of missing data (90 percent or more missing values), see the description of the argument selectFewestMissing for more details.

A group is represented by a corresponding row with the fewest number of missing data if selectFewestMissing has been set to TRUE. Often several rows have the same minimum number of missing values (or no missing values) and a representative must be chosen among those rows. In this case we distinguish 2 situations: (1) If a group corresponds to exactly 2 rows then the corresponding row with the highest average is selected if method="maxMean". Alternative methods can be chosen as described in method. (2) If a group corresponds to more than 2 rows, then the function calculates a signed weighted correlation network (with power specified in connectivityPower) among the corresponding rows if connectivityBasedCollapsing=TRUE. Next the function calculates the network connectivity of each row (closely related to the sum or correlations with the other matching rows). Next it chooses the most highly connected row as representative. If connectivityBasedCollapsing=FALSE, then method is used. For both situations, if more than one row has the same value, the first such row is chosen.

Setting thresholdCombine is a special case of this function, as not all ids for a single group are necessarily collapsed—only those with similar expression patterns are collapsed. We suggest using this option when the goal is to decrease the number of ids for computational reasons, but when ALL ids for a single group should not be combined (for example, if two probes could represent different splice variants for the same gene for many genes on a microarray).

Example application: when dealing with microarray gene expression data then the rows of datET may correspond to unique probe identifiers and rowGroup may contain corresponding gene symbols. Recall that multiple probes (specified using rowID=ProbeID) may correspond to the same gene symbol (specified using rowGroup=GeneSymbol). In this case, datET contains the input expression data with rows as rowIDs and output expression data with rows as gene symbols, collapsing all probes for a given gene symbol into one representative.

Value

The output is a list with the following components.

datETcollapsed is a numeric matrix with the same columns as the input matrix datET, but with

rows corresponding to the different row groups rather than individual row identifiers. (If thresholdCombine is set, then rows still correspond to individual row

identifiers.)

group2row is a matrix whose rows correspond to the unique group labels and whose 2

columns report which group label (first column called group) is represented by what row label (second column called selectedRowID). Set to NULL if

method="ME" or "function".

selectedRow

is a logical vector whose components are TRUE for probes selected as represen-

tatives and FALSE otherwise. It has the same length as the vector probeID. Set

to NULL if method="ME" or "function".

Author(s)

Jeremy A. Miller, Steve Horvath, Peter Langfelder, Chaochao Cai

References

Miller JA, Langfelder P, Cai C, Horvath S (2010) Strategies for optimally aggregating gene expression data: The collapseRows R function. Technical Report.

Examples

```
# seed module eigenvector for the simulateModule function
MEtrue=rnorm(m)
 # numeric data frame of n rows and m columns
datNumeric=data.frame(t(simulateModule(MEtrue,n)))
RowIdentifier=paste("Probe", 1:n, sep="")
ColumnName=paste("Sample",1:m, sep="")
 dimnames(datNumeric)[[2]]=ColumnName
 # Let us now generate a data frame whose first column contains the rowID
 dat1=data.frame(RowIdentifier, datNumeric)
#we simulate a vector with n/5 group labels, i.e. each row group corresponds to 5 rows
 rowGroup=rep( paste("Group",1:(n/5), sep=""), 5 )
 # Typical Input Data
# Since the first column of dat1 contains the RowIdentifier, we use the following code
datET=dat1[,-1]
 rowID=dat1[,1]
 # assign row names according to the RowIdentifier
 dimnames(datET)[[1]]=rowID
 # run the function and save it in an object
collapse.object=collapseRows(datET=datET, rowGroup=rowGroup, rowID=rowID)
 # this creates the collapsed data where
 # the first column contains the group name
# the second column reports the corresponding selected row name (the representative)
 # and the remaining columns report the values of the representative row
dat1Collapsed=data.frame( collapse.object$group2row, collapse.object$datETcollapsed)
 dat1Collapsed[1:5,1:5]
 # EXAMPLE 2:
# Using the same data frame as above, run collapseRows with a user-inputted function.
# In this case we will use the mean. Note that since we are choosing some combination
   of the probe values for each gene, the group2row and selectedRow output
    parameters are not meaningful.
collapse.object.mean=collapseRows(datET=datET, rowGroup=rowGroup, rowID=rowID,
      method="function", methodFunction=colMeans)[[1]]
# Note that in this situation, running the following code produces the identical results:
 collapse.object.mean.2=collapseRows(datET=datET, rowGroup=rowGroup, rowID=rowID,
      method="Average")[[1]]
 # FXAMPLE 3:
 # Using collapseRows to calculate the module eigengene.
 # First we create some sample data as in example 1 (or use your own!)
m=60
n=500
MEtrue=rnorm(m)
```

```
datNumeric=data.frame(t(simulateModule(MEtrue,n)))
 # In this example, rows are genes, and groups are modules.
 RowIdentifier=paste("Gene", 1:n, sep="")
 ColumnName=paste("Sample",1:m, sep="")
 dimnames(datNumeric)[[2]]=ColumnName
 dat1=data.frame(RowIdentifier, datNumeric)
 # We simulate a vector with n/100 modules, i.e. each row group corresponds to 100 rows
 rowGroup=rep( paste("Module",1:(n/100), sep=""), 100 )
 datET=dat1[,-1]
 rowID=dat1[,1]
 dimnames(datET)[[1]]=rowID
 # run the function and save it in an object
collapse.object.ME=collapseRows(datET=datET, rowGroup=rowGroup, rowID=rowID, method="ME")[[1]]
# Note that in this situation, running the following code produces the identical results:
 collapse.object.ME.2 = t(moduleEigengenes(expr=t(datET),colors=rowGroup)$eigengene)
 colnames(collapse.object.ME.2) = ColumnName
 rownames(collapse.object.ME.2) = sort(unique(rowGroup))
```

collapseRowsUsingKME

Selects one representative row per group based on kME

Description

This function selects only the most informative probe for each gene in a kME table, only keeping the probe which has the highest kME with respect to any module in the module membership matrix. This function is a special case of the function collapseRows.

Usage

```
collapseRowsUsingKME(MM, Gin, Pin = NULL, kMEcols = 1:dim(MM)[2])
```

Arguments

ММ	A module membership (kME) table with at least a subset of the columns corresponding to kME values.
Gin	Genes labels in a 1 to 1 correspondence with the rows of MM.
Pin	If NULL (default), rownames of MM are assumed to be probe IDs. If entered, Pin must be the same length as Gin and correspond to probe IDs for MM.
kMEcols	A numeric vector showing which columns in MM correspond to kME values. The default is all of them.

collectGarbage 87

Value

datETcollapsed A numeric matrix with the same columns as the input matrix MM, but with rows

corresponding to the genes rather than the probes.

group2row A matrix whose rows correspond to the unique gene labels and whose 2 columns

report which gene label (first column called group) is represented by what probe

(second column called selectedRowID)

selectedRow A logical vector whose components are TRUE for probes selected as represen-

tatives and FALSE otherwise. It has the same length as the vector Pin.

Author(s)

Jeremy Miller

See Also

collapseRows

Examples

```
# Example: first simulate some data
set.seed(100)
ME.A = sample(1:100,50); ME.B = sample(1:100,50)
ME.C = sample(1:100,50); ME.D = sample(1:100,50)
       = data.frame(ME.A, ME.B, ME.C, ME.D)
simDatA = simulateDatExpr(ME1,1000,c(0.2,0.1,0.08,0.05,0.3), signed=TRUE)
simDatB = simulateDatExpr(ME1, 1000, c(0.2, 0.1, 0.08, 0.05, 0.3), signed=TRUE)
        = c(colnames(simDatA$datExpr),colnames(simDatB$datExpr))
        = paste("Probe",1:length(Gin),sep=".")
Pin
datExpr = cbind(simDatA$datExpr, simDatB$datExpr)
        = corAndPvalue(datExpr,ME1)$cor
# Now run the function and see some example output
results = collapseRowsUsingKME(MM, Gin, Pin)
head(results$MMcollapsed)
head(results$group2Row)
head(results$selectedRow)
```

collectGarbage

Iterative garbage collection.

Description

Performs garbage collection until free memory idicators show no change.

Usage

```
collectGarbage()
```

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Value

None.

Author(s)

Steve Horvath

colQuantileC

Fast colunm- and row-wise quantile of a matrix.

Description

Fast calculation of column- and row-wise quantiles of a matrix at a single probability. Implemented via compiled code, it is much faster than the equivalent apply(data, 2, quantile, prob = p).

Usage

```
colQuantileC(data, p)
rowQuantileC(data, p)
```

Arguments

data a numerical matrix column-wise quantiles are desired. Missing values are re-

moved.

p a single probability at which the quantile is to be calculated.

Details

At present, only one quantile type is implemented, namely the default type 7 used by R.

Value

A vector of length equal the number of columns (for colQuantileC) or rows (for rowQuantileC) in data containing the column- or row-wise quantiles.

Author(s)

Peter Langfelder

See Also

quantile; pquantile for another way of calculating quantiles across structured data.

conformityBasedNetworkConcepts

Calculation of conformity-based network concepts.

Description

This function computes 3 types of network concepts (also known as network indices or statistics) based on an adjacency matrix and optionally a node significance measure.

Usage

conformityBasedNetworkConcepts(adj, GS = NULL)

Arguments

adj adjacency matrix. A symmetric matrix with components between 0 and 1.

optional node significance measure. A vector with length equal the dimension

of adj.

Details

This function computes 3 types of network concepts (also known as network indices or statistics) based on an adjacency matrix and optionally a node significance measure. Specifically, it computes I) fundamental network concepts, II) conformity based network concepts, and III) approximate conformity based network concepts. These network concepts are defined for any symmetric adjacency matrix (weighted and unweighted). The network concepts are described in Dong and Horvath (2007) and Horvath and Dong (2008). In the following, we use the term gene and node interchangeably since these methods were originally developed for gene networks. In the following, we briefly describe the 3 types of network concepts:

Type I: fundamental network concepts are defined as a function of the off-diagonal elements of an adjacency matrix A and/or a node significance measure GS. Type II: conformity-based network concepts are functions of the off-diagonal elements of the conformity based adjacency matrix A.CF=CF*t(CF) and/or the node significance measure. These network concepts are defined for any network for which a conformity vector can be defined. Details: For any adjacency matrix A, the conformity vector CF is calculated by requiring that A[i,j] is approximately equal to CF[i]*CF[j]. Using the conformity one can define the matrix A.CF=CF*t(CF) which is the outer product of the conformity vector with itself. In general, A.CF is not an adjacency matrix since its diagonal elements are different from 1. If the off-diagonal elements of A.CF are similar to those of A according to the Frobenius matrix norm, then A is approximately factorizable. To measure the factorizability of a network, one can calculate the Factorizability, which is a number between 0 and 1 (Dong and Horvath 2007). The conformity is defined using a monotonic, iterative algorithm that maximizes the factorizability measure. Type III: approximate conformity based network concepts are functions of all elements of the conformity based adjacency matrix A.CF (including the diagonal) and/or the node significance measure GS. These network concepts are very useful for deriving relationships between network concepts in networks that are approximately factorizable.

Value

A list with the following components:

Factorizability

number between 0 and 1 giving the factorizability of the matrix. The closer to 1 the higher the evidence of factorizability, that is, A-I is close to outer(CF,CF)diag(CF^2).

fundamental NCs fundamental network concepts, that is network concepts calculated directly from the given adjacency matrix adj. A list with components ScaledConnectivity (giving the scaled connectivity of each node), Connectivity (connectivity of each node), ClusterCoef (the clustering coefficient of each node), MAR (maximum adjacency ratio of each node), Density (the mean density of the network), Centralization (the centralization of the network), Heterogeneity (the heterogeneity of the network). If the input node significance GS is specified, the following additional components are included: NetworkSignificance (network significance, the mean node significance), and HubNodeSignificance (hub node significance given by the linear regression of node significance on connectivity).

conformityBasedNCs

network concepts based on an approximate adjacency matrix given by the outer product of the conformity vector but with unit diagonal. A list with components Conformity (the conformity vector) and Connectivity. CF, ClusterCoef. CF, MAR.CF, Density.CF, Centralization.CF, Heterogeneity.CF giving the conformitybased analogs of the above network concepts.

approximateConformityBasedNCs

network concepts based on an approximate adjacency matrix given by the outer product of the conformity vector. A list with components Conformity (the conformity vector) and Connectivity. CF. App, ClusterCoef. CF. App, MAR. CF. App, Density.CF.App, Centralization.CF.App, Heterogeneity.CF.App giving the conformity-based analogs of the above network concepts.

Author(s)

Steve Horvath

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24 Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

See Also

networkConcepts for calculation of eigennode based network concepts for a correlation network; fundamentalNetworkConcepts for calculation of fundamental network concepts only.

conformityDecomposition

Conformity and module based decomposition of a network adjacency matrix.

Description

The function calculates the conformity based approximation A.CF of an adjacency matrix and a factorizability measure Factorizability. If a module assignment C1 is provided, it also estimates a corresponding intermodular adjacency matrix. In this case, function automatically carries out the module- and conformity based decomposition of the adjacency matrix described in chapter 2 of (Horvath 2011).

Usage

conformityDecomposition(adj, Cl = NULL)

Arguments

adj a symmetric numeric matrix (or data frame) whose entries lie between 0 and 1.

a vector (or factor variable) of length equal to the number of rows of adj. The

variable assigns each network node (row of adj) to a module. The entries of Cl could be integers or character strings.

Details

We distinguish two situation depending on whether or not C1 equals NULL. 1) Let us start out assuming that C1 = NULL. In this case, the function calculates the conformity vector for a general, possibly non-factorizable network adj by minimizing a quadratic (sums of squares) loss function. The conformity and factorizability for an adjacency matrix is defined in (Dong and Horvath 2007, Horvath and Dong 2008) but we briefly describe it in the following. A network is called exactly factorizable if the pairwise connection strength (adjacency) between 2 network nodes can be factored into node specific contributions, named node 'conformity', i.e. if adj[i,j]=Conformity[i]*Conformity[j]. The conformity turns out to be highly related to the network connectivity (aka degree). If adj is not exactly factorizable, then the function conformityDecomposition calculates a conformity vector of the exactly factorizable network that best approximates adj. The factorizability measure Factorizability is a number between 0 and 1. The higher Factorizability, the more factorizable is adj. Warning: the algorithm may only converge to a local optimum and it may not converge at all. Also see the notes below.

2) Let us now assume that C1 is not NULL, i.e. it specifies the module assignment of each node. Then the function calculates a module- and CF-based approximation of adj (explained in chapter 2 in Horvath 2011). In this case, the function calculates a conformity vector Conformity and a matrix IntermodularAdjacency such that adj[i,j] is approximately equal to Conformity[i]*Conformity[j]*IntermodularAdwhere module.index[i] is the row of the matrix IntermodularAdjacency that corresponds to the module assigned to node i. To estimate Conformity and a matrix IntermodularAdjacency, the function attempts to minimize a quadratic loss function (sums of squares). Currently, the function only implements a heuristic algorithm for optimizing the objective function (chapter 2 of Horvath

2011). Another, more accurate Majorization Minorization (MM) algorithm for the decomposition is implemented in the function propensityDecomposition by Ranola et al (2011).

Value

A.CF a symmetric matrix that approximates the input matrix adj. Roughly speaking,

 $the\ i,j-the\ element\ of\ the\ matrix\ equals\ Conformity \ [i] * Conformity \ [j] * Intermodular Adjacency \ [model of\ conformity] = for\ conformity \ [i] = for\ conform$

 $where \ module.index[i] is the row of the \ matrix \ Intermodular Adjacency \ that$

corresponds to the module assigned to node i.

Conformity a numeric vector whose entries correspond to the rows of adj. If C1=NULL then

Conformity[i] is the conformity. If Cl is not NULL then Conformity[i] is

the intramodular conformity with respect to the module that node i belongs to.

IntermodularAdjacency

a symmetric matrix (data frame) whose rows and columns correspond to the number of modules specified in C1. Interpretation: it measures the similarity (adjacency) between the modules. In this case, the rows (and columns) of

Intermodular Adjacency correspond to the entries of Cl.level.

Factorizability

is a number between 0 and 1. If C1=NULL then it equals 1, if (and only if) adj is exactly factorizable. If C1 is a vector, then it measures how well the module-

and CF based decomposition approximates adj.

C1.level is a vector of character strings which correspond to the factor levels of the mod-

ule assignment Cl. Incidentally, the function automatically turns Cl into a factor variable. The components of Conformity and IntramodularFactorizability

correspond to the entries of Cl.level.

IntramodularFactorizability

is a numeric vector of length equal to the number of modules specified by C1. Its entries report the factorizability measure for each module. The components

correspond to the entries of Cl.level.

listConformity

Note

Regarding the situation when C1=NULL. One can easily show that the conformity vector is not unique if adj contains only 2 nodes. However, for more than 2 nodes the conformity is uniquely defined when dealing with an exactly factorizable weighted network whose entries adj[i,j] are larger than 0. In this case, one can get explicit formulas for the conformity (Dong and Horvath 2007).

Author(s)

Steve Horvath

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules. BMC Systems Biology 2007, June 1:24 Horvath S, Dong J (2008) Geometric Interpretation of Gene Co-Expression Network Analysis. PloS Computational Biology. 4(8): e1000117. PMID: 18704157 Horvath S (2011) Weighted Network Analysis. Applications in Genomics and Systems Biology. Springer Book.

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ISBN: 978-1-4419-8818-8 Ranola JMO, Langfelder P, Song L, Horvath S, Lange K (2011) An MM algorithm for the module- and propensity based decomposition of a network. Currently a draft.

See Also

conformityBasedNetworkConcepts

Examples

```
# assume the number of nodes can be divided by 2 and by 3
# here is a perfectly factorizable matrix
A=matrix(1,nrow=n,ncol=n)
# this provides the conformity vector and factorizability measure
conformityDecomposition(adj=A)
# now assume we have a class assignment
Cl=rep(c(1,2),c(n/2,n/2))
conformityDecomposition(adj=A,Cl=Cl)
# here is a block diagonal matrix
blockdiag.A=A
blockdiag.A[1:(n/3),(n/3+1):n]=0
blockdiag.A[(n/3+1):n, 1:(n/3)]=0
block.Cl=rep(c(1,2),c(n/3,2*n/3))
conformityDecomposition(adj= blockdiag.A,Cl=block.Cl)
# another block diagonal matrix
blockdiag.A=A
blockdiag.A[1:(n/3),(n/3+1):n]=0.3
blockdiag.A[(n/3+1):n, 1:(n/3)]=0.3
block.Cl=rep(c(1,2),c(n/3,2*n/3))
conformityDecomposition(adj= blockdiag.A,Cl=block.Cl)
```

consensusCalculation Calculation of a (single) consenus with optional data calibration.

Description

This function calculates a single consensus from given individual data, optionally first calibrating the individual data to make them comparable.

Usage

```
consensusCalculation(
  individualData,
  consensusOptions,

  useBlocks = NULL,
  randomSeed = NULL,
```

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```
saveCalibratedIndividualData = FALSE,
calibratedIndividualDataFilePattern = "calibratedIndividualData-%a-Set%s-Block%b.RData",

# Return options: the data can be either saved or returned but not both.
saveConsensusData = NULL,
consensusDataFileNames = "consensusData-%a-Block%b.RData",
getCalibrationSamples= FALSE,

# Internal handling of data
useDiskCache = NULL, chunkSize = NULL,
cacheDir = ".",
cacheBase = ".blockConsModsCache",

# Behaviour
collectGarbage = FALSE,
verbose = 1, indent = 0)
```

Arguments

individualData Individual data from which the consensus is to be calculated. It can be either a

list or a multiData structure. Each element in individulData can in turn either be a numeric obeject (vector, matrix or array) or a BlockwiseData structure.

consensusOptions

A list of class ConsensusOptions that contains options for the consensus calculation. A suitable list can be obtained by calling function newConsensusOptions.

useBlocks

When individualData contains BlockwiseData, this argument can be an integer vector with indices of blocks for which the calculation should be performed.

randomSeed

If non-NULL, the function will save the current state of the random generator, set the given seed, and restore the random seed to its original state upon exit. If NULL, the seed is not set nor is it restored on exit.

saveCalibratedIndividualData

Logical: should calibrated individual data be saved?

calibratedIndividualDataFilePattern

Pattern from which file names for saving calibrated individual data are determined. The conversions %a, %s and %b will be replaced by analysis name, set number and block number, respectively.

saveConsensusData

Logical: should final consensus be saved (TRUE) or returned in the return value (FALSE)? If NULL, data will be saved only if input data were blockwise data saved on disk rather than held in memory

consensusDataFileNames

Pattern from which file names for saving the final consensus are determined. The conversions %a and %b will be replaced by analysis name and block number, respectively.

getCalibrationSamples

When calibration method in the consensusOptions component of ConsensusTree

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is "single quantile", this logical argument determines whether the calibration samples should be retuned within the return value.

useDiskCache Logical: should disk cache be used for consensus calculations? The disk cache

can be used to sture chunks of calibrated data that are small enough to fit one chunk from each set into memory (blocks may be small enough to fit one block of one set into memory, but not small enogh to fit one block from all sets in a consensus calculation into memory at the same time). Using disk cache is slower but lessens the memry footprint of the calculation. As a general guide, if individual data are split into blocks, we recommend setting this argument to TRUE. If this argument is NULL, the function will decide whether to use disk cache

based on the number of sets and block sizes.

chunkSize Integer giving the chunk size. If left NULL, a suitable size will be chosen auto-

matically.

cacheDir Directory in which to save cache files. The files are deleted on normal exit but

persist if the function terminates abnormally.

cacheBase Base for the file names of cache files.

collectGarbage Logical: should garbage collection be forced after each major calculation?

verbose Integer level of verbosity of diagnostic messages. Zero means silent, higher

values make the output progressively more and more verbose.

indent Indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

Consensus is defined as the element-wise (also known as "parallel") quantile of the individual data at probability given by the consensusQuantile element of consensusOptions. Depending on the value of component calibration of consensusOptions, the individual data are first calibrated. For consensusOptions\$calibration="full quantile", the individual data are quantile normalized using normalize.quantiles. For consensusOptions\$calibration="single quantile", the individual data are raised to a power such that the quantiles at probability consensusOptions\$calibrationQuantile are the same. For consensusOptions\$calibration="none", the individual data are not calibrated.

Value

A list with the following components:

 ${\tt consensusData} \quad A \; {\tt BlockwiseData} \; \; {\tt list} \; {\tt containing} \; {\tt the} \; {\tt consensus}.$

nSets Number of input data sets.

saveCalibratedIndividualData

Copy of the input saveCalibratedIndividualData.

calibratedIndividualData

If input saveCalibratedIndividualData is TRUE, a list in which each component is a BlockwiseData structure containing the calibrated individual data for the corresponding input individual data set.

calibrationSamples

If consensusOptions\$calibration is "single quantile" and getCalibrationSamples

is TRUE, a list in which each component contains the calibration samples for the

corresponding input individual data set.

originCount A vector of length nSets that contains, for each set, the number of (calibrated)

elements that were less than or equal the consensus for that element.

Author(s)

Peter Langfelder

References

Consensus network analysis was originally described in Langfelder P, Horvath S. Eigengene networks for studying the relationships between co-expression modules. BMC Systems Biology 2007, 1:54 https://bmcsystbiol.biomedcentral.com/articles/10.1186/1752-0509-1-54

See Also

normalize.quantiles for quantile normalization.

consensusDissTOMandTree

Consensus clustering based on topological overlap and hierarchical clustering

Description

This function makes a consensus network using all of the default values in the WGCNA library. Details regarding how consensus modules are formed can be found here: http://horvath.genetics.ucla.edu/html/CoexpressionNetNetworkConstruction-man.pdf

Usage

consensusDissTOMandTree(multiExpr, softPower, TOM = NULL)

Arguments

multiExpr Expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data. Rows correspond to samples and columns to genes or probes. Two or

more sets of data must be included and adjacencies cannot be used.

softPower Soft thresholding power used to make each of the networks in multiExpr.

TOM A LIST of matrices holding the topological overlap corresponding to the sets

in multiExpr, if they have already been calculated. Otherwise, keep TOM set as NULL (default), and TOM similarities will be calculated using the WGCNA defaults. If inputted, this variable must be a list with each entree a TOM corre-

sponding to the same entries in multiExpr.

Value

consensusTOM The TOM difference matrix (1-TOM similarity) corresponding to the consensus

network.

consTree Returned value is the same as that of hclust: An object of class hclust which

describes the tree produced by the clustering process. This tree corresponds to

the dissimilarity matrix consensusTOM.

Author(s)

Peter Langfelder, Steve Horvath, Jeremy Miller

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

blockwiseConsensusModules

Examples

```
# Example consensus network using two simulated data sets
set.seed
           = 100
MEturquoise = sample(1:100,50)
MEblue
         = sample(1:100,50)
MEbrown
           = sample(1:100,50)
MEyellow = sample(1:100,50)
MEgreen
           = sample(1:100,50)
ME = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen)
system.time({
dat1 = simulateDatExpr(ME,300,c(0.2, 0.10, 0.10, 0.10, 0.10, 0.2), signed=TRUE)})
system.time({
dat2 = simulateDatExpr(ME,300,c(0.18, 0.11, 0.11, 0.09, 0.11, 0.23),signed=TRUE)})
multiExpr = list(S1=list(data=dat1$datExpr),S2=list(data=dat2$datExpr))
softPower=8
system.time( {
consensusNetwork = consensusDissTOMandTree(multiExpr, softPower)})
system.time({
plotDendroAndColors(consensusNetwork$consTree, cbind(labels2colors(dat1$allLabels),
     labels2colors(dat2$allLabels)),c("S1","S2"), dendroLabels=FALSE)})
```

consensusKME	Calculate consensus kME (eigengene-based connectivities) across multiple data sets.

Description

Calculate consensus kME (eigengene-based connectivities) across multiple data sets, typically following a consensus module analysis.

Usage

```
consensusKME(
  multiExpr,
  moduleLabels,
  multiEigengenes = NULL,
  consensusQuantile = 0,
  signed = TRUE,
  useModules = NULL,
  metaAnalysisWeights = NULL,
  corAndPvalueFnc = corAndPvalue, corOptions = list(), corComponent = "cor",
  getQvalues = FALSE,
  useRankPvalue = TRUE,
  rankPvalueOptions = list(calculateQvalue = getQvalues, pValueMethod = "scale"),
  setNames = NULL,
  excludeGrey = TRUE,
  greyLabel = if (is.numeric(moduleLabels)) 0 else "grey")
```

Arguments

multiExpr Expression (or other numeric) data in a multi-set format. A vector of lists; in

each list there must be a component named 'data' whose content is a matrix or

dataframe or array of dimension 2.

moduleLabels Module labels: one label for each gene in multiExpr.

multiEigengenes

Optional eigengenes of modules specified in moduleLabels. If not given, will

be calculated from multiExpr.

signed logical: should the network be considered signed? In signed networks (TRUE),

negative kME values are not considered significant and the corresponding p-values will be one-sided. In unsigned networks (FALSE), negative kME values are considered significant and the corresponding p-values will be two-sided.

useModules Optional specification of module labels to which the analysis should be re-

stricted. This could be useful if there are many modules, most of which are not interesting. Note that the "grey" module cannot be used with useModules.

consensusQuantile

Quantile for the consensus calculation. Should be a number between 0 (minimum) and 1.

metaAnalysisWeights

Optional specification of meta-analysis weights for each input set. If given, must be a numeric vector of length equal the number of input data sets (i.e., length(multiExpr)). These weights will be used in addition to constant weights and weights proportional to number of samples (observations) in each set.

corAndPvalueFnc

Function that calculates associations between expression profiles and eigen-

genes. See details.

corOptions List giving additional arguments to function corAndPvalueFnc. See details.

corComponent Name of the component of output of corAndPvalueFnc that contains the actual

correlation.

getQvalues logical: should q-values (estimates of FDR) be calculated?

useRankPvalue Logical: should the rankPvalue function be used to obtain alternative meta-

analysis statistics?

rankPvalueOptions

Additional options for function rankPvalue. These include na.last (default "keep"), ties.method (default "average"), calculateQvalue (default copied from input getQvalues), and pValueMethod (default "scale"). See the help

file for rankPvalue for full details.

setNames names for the input sets. If not given, will be taken from names (multiExpr). If

those are NULL as well, the names will be "Set_1", "Set_2",

excludeGrey logical: should the grey module be excluded from the kME tables? Since the

grey module is typically not a real module, it makes little sense to report kME

values for it.

greyLabel label that labels the grey module.

Details

The function corAndPvalueFnc is currently is expected to accept arguments x (gene expression profiles), y (eigengene expression profiles), and alternative with possibilities at least "greater", "two.sided". Any additional arguments can be passed via corOptions.

The function corAndPvalueFnc should return a list which at the least contains (1) a matrix of associations of genes and eigengenes (this component should have the name given by corComponent), and (2) a matrix of the corresponding p-values, named "p" or "p.value". Other components are optional but for full functionality should include (3) nObs giving the number of observations for each association (which is the number of samples less number of missing data - this can in principle vary from association to association), and (4) Z giving a Z static for each observation. If these are missing, nObs is calculated in the main function, and calculations using the Z statistic are skipped.

Value

Data frame with the following components (for easier readability the order here is not the same as in the actual output):

ID Gene ID, taken from the column names of the first input data set

consensus.kME.1, consensus.kME.2, ...

Consensus kME (that is, the requested quantile of the kMEs in the individual data sets)in each module for each gene across the input data sets. The module labels (here 1, 2, etc.) correspond to those in moduleLabels.

weightedAverage.equalWeights.kME1, weightedAverage.equalWeights.kME2,

. . .

Average kME in each module for each gene across the input data sets.

weightedAverage.RootDoFWeights.kME1,weightedAverage.RootDoFWeights.kME2,

. . .

Weighted average kME in each module for each gene across the input data sets. The weight of each data set is proportional to the square root of the number of samples in the set.

weightedAverage.DoFWeights.kME1, weightedAverage.DoFWeights.kME2,

. . .

Weighted average kME in each module for each gene across the input data sets. The weight of each data set is proportional to number of samples in the set.

 $weighted \verb|Average.userWeights.kME1|, weighted \verb|Average.userWeights.kME2|,$

. . .

(Only present if input metaAnalysisWeights is non-NULL.) Weighted average kME in each module for each gene across the input data sets. The weight of each data set is given in metaAnalysisWeights.

meta.Z.equalWeights.kME1, meta.Z.equalWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set equally. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.Z.RootDoFWeights.kME1, meta.Z.RootDoFWeights.kME2, . . .

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by the square root of the number of samples. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.Z.DoFWeights.kME1, meta.Z.DoFWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by the number of samples. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.Z.userWeights.kME1, meta.Z.userWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by metaAnalysisWeights. Only returned if metaAnalysisWeights is non-NULL and the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.p.equalWeights.kME1, meta.p.equalWeights.kME2, ...

p-values obtained from the equal-weight meta-analysis Z statistics. Only returned if the function <code>corAndPvalueFnc</code> returns the Z statistics corresponding to the correlations.

meta.p.RootDoFWeights.kME1, meta.p.RootDoFWeights.kME2, ...

p-values obtained from the meta-analysis Z statistics with weights proportional to the square root of the number of samples. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.p.DoFWeights.kME1, meta.p.DoFWeights.kME2, ...

p-values obtained from the degree-of-freedom weight meta-analysis Z statistics. Only returned if the function <code>corAndPvalueFnc</code> returns the Z statistics corresponding to the correlations.

meta.p.userWeights.kME1, meta.p.userWeights.kME2, ...

p-values obtained from the user-supplied weight meta-analysis Z statistics. Only returned if metaAnalysisWeights is non-NULL and the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.q.equalWeights.kME1, meta.q.equalWeights.kME2, ...

q-values obtained from the equal-weight meta-analysis p-values. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.RootDoFWeights.kME1, meta.q.RootDoFWeights.kME2, ...

q-values obtained from the meta-analysis p-values with weights proportional to the square root of the number of samples. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.DoFWeights.kME1, meta.q.DoFWeights.kME2, ...

q-values obtained from the degree-of-freedom weight meta-analysis p-values. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.userWeights.kME1, meta.q.userWeights.kME2, ...

q-values obtained from the user-specified weight meta-analysis p-values. Only present if metaAnalysisWeights is non-NULL, getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

The next set of columns contain the results of function rankPvalue and are only present if input useRankPvalue is TRUE. Some columns may be missing depending on the options specified in rankPvalueOptions. We explicitly list columns that are based on weighing each set equally; names of these columns carry the suffix .equalWeights

pValue Extreme Rank. ME 1. equal Weights, pValue Extreme Rank. ME 2. equal Weights,

This is the minimum between pValueLowRank and pValueHighRank, i.e. min(pValueLow, pValueHigh)

Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

 ${\tt pValueHighRank.ME1.equalWeights, pValueHighRank.ME2.equalWeights,}$

Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

pValueExtremeScale.ME1.equalWeights,pValueExtremeScale.ME2.equalWeights,

This is the minimum between pValueLowScale and pValueHighScale, i.e. min(pValueLow, pValueHigh)

```
pValueLowScale.ME1.equalWeights,
                                       pValueLowScale.ME2.equalWeights,
                 Asymptotic p-value for observing a consistently low value across the columns
                 of datS based on the Scale method.
pValueHighScale.ME1.equalWeights, pValueHighScale.ME2.equalWeights,
                 Asymptotic p-value for observing a consistently low value across the columns
                 of datS based on the Scale method.
qValueExtremeRank.ME1.equalWeights,qValueExtremeRank.ME2.equalWeights,
                 local false discovery rate (q-value) corresponding to the p-value pValueExtremeR-
                 ank
qValueLowRank.ME1.equalWeights, qValueLowRank.ME2.equalWeights, ...
                 local false discovery rate (q-value) corresponding to the p-value pValueLowRank
qValueHighRank.ME1.equalWeights, lueHighRank.ME2.equalWeights, ...
                 local false discovery rate (q-value) corresponding to the p-value pValueHigh-
                 Rank
qValueExtremeScale.ME1.equalWeights,qValueExtremeScale.ME2.equalWeights,
                 local false discovery rate (q-value) corresponding to the p-value pValueExtremeScale
qValueLowScale.ME1.equalWeights,
                                       qValueLowScale.ME2.equalWeights,
                 local false discovery rate (q-value) corresponding to the p-value pValueLowS-
qValueHighScale.ME1.equalWeights, qValueHighScale.ME2.equalWeights,
                 local false discovery rate (q-value) corresponding to the p-value pValueHigh-
                 Scale
                 Analogous columns corresponding to weighing individual sets by the square
                 root of the number of samples, by number of samples, and by user weights
                 (if given). The corresponding column name suffixes are .RootDoFWeights,
                 .DoFWeights, and .userWeights.
The following set of columns summarize kME in individual input data sets.
kME1.Set_1, kME1.Set_2, ..., kME2.Set_1, kME2.Set_2, ...
                 kME values for each gene in each module in each given data set.
p.kME1.Set_1, p.kME1.Set_2, ..., p.kME2.Set_1, p.kME2.Set_2, ...
                 p-values corresponding to kME values for each gene in each module in each
                 given data set.
g.kME1.Set_1, g.kME1.Set_2, ..., g.kME2.Set_1, g.kME2.Set_2, ...
                 q-values corresponding to kME values for each gene in each module in each
                 given data set. Only returned if getQvalues is TRUE.
Z.kME1.Set_1, Z.kME1.Set_2, ..., Z.kME2.Set_1, Z.kME2.Set_2, ...
                 Z statistics corresponding to kME values for each gene in each module in each
                 given data set. Only present if the function corAndPvalueFnc returns the Z
                 statistics corresponding to the kME values.
```

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S., WGCNA: an R package for weighted correlation network analysis. BMC Bioinformatics. 2008 Dec 29; 9:559.

See Also

signedKME for eigengene based connectivity in a single data set. corAndPvalue, bicorAndPvalue for two alternatives for calculating correlations and the corresponding p-values and Z scores. Both can be used with this function.

consensusMEDissimilarity

Consensus dissimilarity of module eigengenes.

Description

Calculates consensus dissimilarity (1-cor) of given module eigengenes realized in several sets.

Usage

consensusMEDissimilarity(MEs, useAbs = FALSE, useSets = NULL, method = "consensus")

Arguments

MEs	Module eigengenes of the same modules in several sets.
useAbs	Controls whether absolute value of correlation should be used instead of correlation in the calculation of dissimilarity.
useSets	If the consensus is to include only a selection of the given sets, this vector (or scalar in the case of a single set) can be used to specify the selection. If NULL, all sets will be used.
method	A character string giving the method to use. Allowed values are (abbreviations of) "consensus" and "majority". The consensus dissimilarity is calculated as the minimum of given set dissimilarities for "consensus" and as the average for "majority".

Details

This function calculates the individual set dissimilarities of the given eigengenes in each set, then takes the (parallel) maximum or average over all sets. For details on the structure of imput data, see checkSets.

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Value

A dataframe containing the matrix of dissimilarities, with names and rownames set appropriately.

Author(s)

```
Peter Langfelder, <Peter.Langfelder@gmail.com>
```

See Also

checkSets

consensusOrderMEs

Put close eigenvectors next to each other in several sets.

Description

Reorder given (eigen-)vectors such that similar ones (as measured by correlation) are next to each other. This is a multi-set version of orderMEs; the dissimilarity used can be of consensus type (for each pair of eigenvectors the consensus dissimilarity is the maximum of individual set dissimilarities over all sets) or of majority type (for each pair of eigenvectors the consensus dissimilarity is the average of individual set dissimilarities over all sets).

Usage

Arguments

MEs	Module eigengenes of several sets in a multi-set format (see checkSets). A vector of lists, with each list corresponding to one dataset and the module eigengenes in the component data, that is MEs[[set]]\$data[sample, module] is the expression of the eigengene of module module in sample sample in dataset set. The number of samples can be different between the sets, but the modules must be the same.
useAbs	Controls whether vector similarity should be given by absolute value of correlation or plain correlation.
useSets	Allows the user to specify for which sets the eigengene ordering is to be performed.
greyLast	Normally the color grey is reserved for unassigned genes; hence the grey module is not a proper module and it is conventional to put it last. If this is not desired, set the parameter to FALSE.
greyName	Name of the grey module eigengene.

method

A character string giving the method to be used calculating the consensus dissimilarity. Allowed values are (abbreviations of) "consensus" and "majority". The consensus dissimilarity is calculated as the maximum of given set dissimilarities for "consensus" and as the average for "majority".

Details

Ordering module eigengenes is useful for plotting purposes. This function calculates the consensus or majority dissimilarity of given eigengenes over the sets specified by useSets (defaults to all sets). A hierarchical dendrogram is calculated using the dissimilarity and the order given by the dendrogram is used for the eigengenes in all other sets.

Value

A vector of lists of the same type as MEs containing the re-ordered eigengenes.

Author(s)

```
Peter Langfelder, <Peter.Langfelder@gmail.com>
```

See Also

```
moduleEigengenes, multiSetMEs, orderMEs
```

consensusProjectiveKMeans

Consensus projective K-means (pre-)clustering of expression data

Description

Implementation of a consensus variant of K-means clustering for expression data across multiple data sets.

Usage

```
consensusProjectiveKMeans(
  multiExpr,
  preferredSize = 5000,
  nCenters = NULL,
  sizePenaltyPower = 4,
  networkType = "unsigned",
  randomSeed = 54321,
  checkData = TRUE,
  imputeMissing = TRUE,
  useMean = (length(multiExpr) > 3),
  maxIterations = 1000,
  verbose = 0, indent = 0)
```

Arguments

multiExpr expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression

data, with rows corresponding to samples and columns to genes or probes.

preferredSize preferred maximum size of clusters.

nCenters number of initial clusters. Empirical evidence suggests that more centers will

give a better preclustering; the default is as.integer(min(nGenes/20, 100*nGenes/preferredSize))

and is an attempt to arrive at a reasonable number given the resources available.

sizePenaltyPower

parameter specifying how severe is the penalty for clusters that exceed preferredSize.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

randomSeed integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit.

checkData logical: should data be checked for genes with zero variance and genes and

samples with excessive numbers of missing samples? Bad samples are ignored;

returned cluster assignment for bad genes will be NA.

imputeMissing logical: should missing values in datExpr be imputed before the calculations

start? If the missing data are not imputed, they will be replaced by 0 which can

be problematic.

useMean logical: should mean distance across sets be used instead of maximum? See

details.

maxIterations maximum iterations to be attempted.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The principal aim of this function within WGCNA is to pre-cluster a large number of genes into smaller blocks that can be handled using standard WGCNA techniques.

This function implements a variant of K-means clustering that is suitable for co-expression analysis.

Cluster centers are defined by the first principal component, and distances by correlation. Consensus distance across several sets is defined as the maximum of the corresponding distances in individual sets; however, if useMean is set, the mean distance will be used instead of the maximum. The distance between a gene and a center of a cluster is multiplied by a factor of $max(clusterSize/preferredSize, 1)^{sizePenaltyPothus}$ thus penalizing clusters whose size exceeds preferredSize. The function starts with randomly generated cluster assignment (hence the need to set the random seed for repeatability) and executes interations of calculating new centers and reassigning genes to nearest (in the consensus sense) center until the clustering becomes stable. Before returning, nearby clusters are iteratively combined if their combined size is below preferredSize.

Consensus distance defined as maximum of distances in all sets is consistent with the approach taken in blockwiseConsensusModules, but the procedure may not converge. Hence it is advisable

to use the mean as consensus in cases where there are multiple data sets (4 or more, say) and/or if the input data sets are very different.

The standard principal component calculation via the function svd fails from time to time (likely a convergence problem of the underlying lapack functions). Such errors are trapped and the principal component is approximated by a weighted average of expression profiles in the cluster. If verbose is set above 2, an informational message is printed whenever this approximation is used.

Value

A list with the following components:

clusters a numerical vector with one component per input gene, giving the cluster num-

ber in which the gene is assigned.

centers a vector of lists, one list per set. Each list contains a component data that

contains a matrix whose columns are the cluster centers in the corresponding

set.

unmergedClusters

a numerical vector with one component per input gene, giving the cluster num-

ber in which the gene was assigned before the final merging step.

unmergedCenters

a vector of lists, one list per set. Each list contains a component data that contains a matrix whose columns are the cluster centers before merging in the

corresponding set.

Author(s)

Peter Langfelder

See Also

projectiveKMeans

consensusRepresentatives

Consensus selection of group representatives

Description

Given multiple data sets corresponding to the same variables and a grouping of variables into groups, the function selects a representative variable for each group using a variety of possible selection approaches. Typical uses include selecting a representative probe for each gene in microarray data.

Usage

```
consensusRepresentatives(
   mdx,
   group,
   colID,
   consensusQuantile = 0,
   method = "MaxMean",
   useGroupHubs = TRUE,
   calibration = c("none", "full quantile"),
   selectionStatisticFnc = NULL,
   connectivityPower = 1,
   minProportionPresent = 1,
   getRepresentativeData = TRUE,
   statisticFncArguments = list(),
   adjacencyArguments = list(),
   verbose = 2, indent = 0)
```

Arguments

mdx A multiData structure. All sets must have the same columns.

group Character vector whose components contain the group label (e.g. a character

string) for each entry of colID. This vector must be of the same length as the vector colID. In gene expression applications, this vector could contain the gene

symbol (or a co-expression module label).

colID Character vector of column identifiers. This must include all the column names

from mdx, but can include other values as well. Its entries must be unique (no

duplicates) and no missing values are permitted.

consensusQuantile

A number between 0 and 1 giving the quantile probability for consensus calculation. 0 means the minimum value (true consensus) will be used.

lation. O means the minimum value (true consensus) will be used

method

character string for determining which method is used to choose the representative (when useGroupHubs is TRUE, this method is only used for groups with 2 variables). The following values can be used: "MaxMean" (default) or "MinMean" return the variable with the highest or lowest mean value, respectively; "maxRowVariance" return the variable with the highest variance; "absMaxMean" or "absMinMean" return the variable with the highest or lowest mean absolute value; and "function" will call a user-input function (see the description of the argument selectionStatisticFnc). The built-in functions can be instructed to use robust analogs (median and median absolute deviation) by also specifying statisticFncArguments=list(robust = TRUE).

useGroupHubs

Logical: if TRUE, groups with 3 or more variables will be represented by the variable with the highest connectivity according to a signed weighted correlation network adjacency matrix among the corresponding rows. The connectivity is defined as the row sum of the adjacency matrix. The signed weighted adjacency matrix is defined as A=(0.5+0.5*COR)^power where power is determined by the argument connectivityPower and COR denotes the matrix of pairwise correlation coefficients among the corresponding rows. Additional

arguments to the underlying function adjacency can be specified using the argument adjacencyArguments below.

calibration

Character string describing the method of calibration of the selection statistic among the data sets. Recognized values are "none" (no calibration) and "full quantile" (quantile normalization).

selectionStatisticFnc

User-supplied function used to calculate the selection statistic when method above equals "function". The function must take argumens x (a matrix) and possibly other arguments that can be specified using statisticFncArguments below. The return value must be a vector with one component per column of x giving the selection statistic for each column.

connectivityPower

Positive number (typically integer) for specifying the soft-thresholding power used to construct the signed weighted adjacency matrix, see the description of useGroupHubs. This option is only used if useGroupHubs is TRUE.

minProportionPresent

A number between 0 and 1 specifying a filter of candidate probes. Specifically, for each group, the variable with the maximum consensus proportion of present data is found. Only variables whose consensus proportion of present data is at least minProportionPresent times the maximum consensus proportion are retained as candidates for being a representative.

getRepresentativeData

Logical: should the representative data, i.e., mdx restricted to the representative variables, be returned?

statisticFncArguments

A list giving further arguments to the selection statistic function. Can be used to supply additional arguments to the user-specified selectionStatisticFnc; the value list(robust = TRUE) can be used with the built-in functions to use their robust variants.

adjacencyArguments

Further arguments to the function adjacency, e.g. adjacencyArguments=list(corFnc = "bicor", corOptions = "use = 'p', maxPOutliers = 0.05") will select the robust correlation bicor with a good set of options. Note that the adjacency arguments type and power cannot be changed.

verbose

Level of verbosity; 0 means silent, larger values will cause progress messages to be printed.

indent

Indent for the diagnostic messages; each unit equals two spaces.

Details

This function was inspired by collapseRows, but there are also important differences. This function focuses on selecting representatives; when summarization is more important, collapseRows provides more flexibility since it does not require that a single representative be selected.

This function and collapseRows use different input and ouput conventions; user-specified functions need to be tailored differently for collapseRows than for consensusRepresentatives.

Missing data are allowed and are treated as missing at random. If rowID is NULL, it is replaced by the variable names in mdx.

All groups with a single variable are represented by that variable, unless the consensus proportion of present data in the variable is lower than minProportionPresent, in which case the variable and the group are excluded from the output.

For all variables belonging to groups with 2 variables (when useGroupHubs=TRUE) or with at least 2 variables (when useGroupHubs=FALSE), selection statistics are calculated in each set (e.g., the selection statistic may be the mean, variance, etc). This results in a matrix of selection statistics (one entry per variable per data set). The selection statistics are next optionally calibrated (normalized) between sets to make them comparable; currently the only implemented calibration method is quantile normalization.

For each variable, the consensus selection statistic is defined as the consensus of the (calibrated) selection statistics across the data sets is calculated. The 'consensus' of a vector (say 'x') is simply defined as the quantile with probability consensusQuantile of the vector x. Important exception: for the "MinMean" and "absMinMean" methods, the consensus is the quantile with probability 1-consensusQuantile, since the idea of the consensus is to select the worst (or close to worst) value across the data sets.

For each group, the representative is selected as the variable with the best (typically highest, but for "MinMean" and "absMinMean" methods the lowest) consensus selection statistic.

If useGroupHubs=TRUE, the intra-group connectivity is calculated for all variables in each set. The intra-group connectivities are optionally calibrated (normalized) between sets, and consensus intra-group connectivity is calculated similarly to the consensus selection statistic above. In each group, the variable with the highest consensus intra-group connectivity is chosen as the representative.

Value

representatives

A named vector giving, for each group, the selected representative (input rowID or the variable (column) name in mdx). Names correspond to groups.

varSelected

A logical vector with one entry per variable (column) in input mdx (possibly after restriction to variables occurring in colID), TRUE if the column was selected as a representative.

representativeData

Only present if getRepresentativeData is TRUE; the input mdx restricted to the representative variables, with column names changed to the corresponding groups.

Author(s)

Peter Langfelder, based on code by Jeremy Miller

See Also

multiData for a description of the multiData structures; collapseRows that solves a related but different problem. Please note the differences in input and output!

consensusTOM

Consensus network (topological overlap).

Description

Calculation of a consensus network (topological overlap).

Usage

```
consensusTOM(
      # Supply either ...
      # ... information needed to calculate individual TOMs
      multiExpr,
      # Data checking options
      checkMissingData = TRUE,
      # Blocking options
      blocks = NULL,
      maxBlockSize = 5000,
      blockSizePenaltyPower = 5,
      nPreclusteringCenters = NULL,
      randomSeed = 54321,
      # Network construction arguments: correlation options
      corType = "pearson",
      maxPOutliers = 1,
      quickCor = 0,
      pearsonFallback = "individual",
      cosineCorrelation = FALSE,
      replaceMissingAdjacencies = FALSE,
      # Adjacency function options
      power = 6,
      networkType = "unsigned",
      checkPower = TRUE,
      # Topological overlap options
      TOMType = "unsigned",
      TOMDenom = "min",
      suppressNegativeTOM = FALSE,
      # Save individual TOMs?
```

```
saveIndividualTOMs = TRUE,
  individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",
  # ... or individual TOM information
  individualTOMInfo = NULL,
  useIndivTOMSubset = NULL,
##### Consensus calculation options
  useBlocks = NULL,
  networkCalibration = c("single quantile", "full quantile", "none"),
  # Save calibrated TOMs?
  saveCalibratedIndividualTOMs = FALSE,
 calibratedIndividualTOMFilePattern = "calibratedIndividualTOM-Set%s-Block%b.RData",
  # Simple quantile calibration options
  calibrationQuantile = 0.95,
  sampleForCalibration = TRUE, sampleForCalibrationFactor = 1000,
  getNetworkCalibrationSamples = FALSE,
  # Consensus definition
  consensusQuantile = 0,
  useMean = FALSE,
  setWeights = NULL,
  # Return options
  saveConsensusTOMs = TRUE,
  consensusTOMFilePattern = "consensusTOM-Block%b.RData",
  returnTOMs = FALSE,
  # Internal handling of TOMs
  useDiskCache = NULL, chunkSize = NULL,
  cacheDir = ".",
  cacheBase = ".blockConsModsCache",
  nThreads = 1,
  # Diagnostic messages
  verbose = 1,
  indent = 0)
```

Arguments

multiExpr

expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

checkMissingData

logical: should data be checked for excessive numbers of missing entries in

genes and samples, and for genes with zero variance? See details.

blocks optional specification of blocks in which hierarchical clustering and module de-

tection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the correspond-

ing gene belongs.

maxBlockSize integer giving maximum block size for module detection. Ignored if blocks

above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not

exceed maxBlockSize.

blockSizePenaltyPower

number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block

size is very important.

nPreclusteringCenters

number of centers for pre-clustering. Larger numbers typically results in better

but slower pre-clustering. The default is as.integer(min(nGenes/20, 100*nGenes/preferredSize))

and is an attempt to arrive at a reasonable number given the resources available.

randomSeed integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit. If NULL is given,

the function will not save and restore the seed.

corType character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pariwise.complete.obs

option.

maxPOutliers only used for corType=="bicor". Specifies the maximum percentile of data

that can be considered outliers on either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar

(but not equal to) Pearson correlation.

quickCor real number between 0 and 1 that controls the handling of missing data in the

calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation, if used, should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE). Has

no effect for Pearson correlation. See bicor.

cosineCorrelation

logical: should the cosine version of the correlation calculation be used? The cosine calculation differs from the standard one in that it does not subtract the

soft-thresholding power for network construction. power

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

logical: should basic sanity check be performed on the supplied power? If you checkPower

would like to experiment with unusual powers, set the argument to FALSE and

proceed with caution.

replaceMissingAdjacencies

logical: should missing values in the calculation of adjacency be replaced by 0?

one of "none", "unsigned", "signed", "signed Nowick", "unsigned 2", "signed **TOMType**

2" and "signed Nowick 2". If "none", adjacency will be used for clustering.

See TOMsimilarityFromExpr for details.

TOMDenom a character string specifying the TOM variant to be used. Recognized values

> are "min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results but at this time should be considered

experimental.

suppressNegativeTOM

Logical: should the result be set to zero when negative? Negative TOM values can occur when TOMType is "signed Nowick".

saveIndividualTOMs

logical: should individual TOMs be saved to disk for later use?

individualTOMFileNames

character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

individualTOMInfo

Optional data for TOM matrices in individual data sets. This object is returned by the function blockwiseIndividualTOMs. If not given, appropriate topological overlaps will be calculated using the network contruction options below.

useIndivTOMSubset

If individualTOMInfo is given, this argument allows to only select a subset of the individual set networks contained in individual TOMInfo. It should be a numeric vector giving the indices of the individual sets to be used. Note that this

argument is NOT applied to multiExpr.

useBlocks optional specification of blocks that should be used for the calcualtions. The

default is to use all blocks.

networkCalibration

network calibration method. One of "single quantile", "full quantile", "none" (or a unique abbreviation of one of them).

saveCalibratedIndividualTOMs

logical: should the calibrated individual TOMs be saved?

calibratedIndividualTOMFilePattern

pattern of file names for saving calibrated individual TOMs.

calibrationQuantile

if networkCalibration is "single quantile", topological overlaps (or adjacencies if TOMs are not computed) will be scaled such that their calibrationQuantile quantiles will agree.

sampleForCalibration

if TRUE, calibration quantiles will be determined from a sample of network similarities. Note that using all data can double the memory footprint of the function and the function may fail.

sampleForCalibrationFactor

determines the number of samples for calibration: the number is 1/calibrationQuantile * sampleForCalibrationFactor. Should be set well above 1 to ensure accuracy of the sampled quantile.

getNetworkCalibrationSamples

logical: should the sampled values used for network calibration be returned?

consensusQuantile

quantile at which consensus is to be defined. See details.

useMean logical: should the consensus be determined from a (possibly weighted) mean

across the data sets rather than a quantile?

setWeights Optional vector (one component per input set) of weights to be used for weighted

mean consensus. Only used when useMean above is TRUE.

saveConsensusTOMs

logical: should the consensus topological overlap matrices for each block be

saved and returned?

consensusTOMFilePattern

character string containing the file namefiles containing the consensus topological overlaps. The tag %b will be replaced by the block number. If the resulting file names are non-unique (for example, because the user gives a file name without a %b tag), an error will be generated. These files are standard R data files and

can be loaded using the load function.

returnTOMs logical: should calculated consensus TOM(s) be returned?

useDiskCache should calculated network similarities in individual sets be temporarilly saved

> to disk? Saving to disk is somewhat slower than keeping all data in memory, but for large blocks and/or many sets the memory footprint may be too big. If not given (the default), the function will determine the need of caching based on the

size of the data. See chunkSize below for additional information.

chunkSize network similarities are saved in smaller chunks of size chunkSize. If NULL, an

> appropriate chunk size will be determined from an estimate of available memory. Note that if the chunk size is greater than the memory required for storing

intemediate results, disk cache use will automatically be disabled.

cacheDir character string containing the directory into which cache files should be written.

The user should make sure that the filesystem has enough free space to hold the

cache files which can get quite large.

cacheBase character string containing the desired name for the cache files. The actual file

names will consists of cacheBase and a suffix to make the file names unique.

nThreads non-negative integer specifying the number of parallel threads to be used by cer-

tain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calcula-

tions will use 2 threads.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The function starts by optionally filtering out samples that have too many missing entries and genes that have either too many missing entries or zero variance in at least one set. Genes that are filtered out are left unassigned by the module detection. Returned eigengenes will contain NA in entries corresponding to filtered-out samples.

If blocks is not given and the number of genes exceeds maxBlockSize, genes are pre-clustered into blocks using the function consensusProjectiveKMeans; otherwise all genes are treated in a single block.

For each block of genes, the network is constructed and (if requested) topological overlap is calculated in each set. To minimize memory usage, calculated topological overlaps are optionally saved to disk in chunks until they are needed again for the calculation of the consensus network topological overlap.

Before calculation of the consensus Topological Overlap, individual TOMs are optionally calibrated. Calibration methods include single quantile scaling and full quantile normalization.

Single quantile scaling raises individual TOM in sets 2,3,... to a power such that the quantiles given by calibrationQuantile agree with the quantile in set 1. Since the high TOMs are usually the most important for module identification, the value of calibrationQuantile is close to (but not equal) 1. To speed up quantile calculation, the quantiles can be determined on a randomly-chosen component subset of the TOM matrices.

Full quantile normalization, implemented in normalize.quantiles, adjusts the TOM matrices such that all quantiles equal each other (and equal to the quantiles of the component-wise average of the individual TOM matrices).

Note that network calibration is performed separately in each block, i.e., the normalizing transformation may differ between blocks. This is necessary to avoid manipulating a full TOM in memory.

The consensus TOM is calculated as the component-wise consensusQuantile quantile of the individual (set) TOMs; that is, for each gene pair (TOM entry), the consensusQuantile quantile across all input sets. Alternatively, one can also use (weighted) component-wise mean across all imput data sets. If requested, the consensus topological overlaps are saved to disk for later use.

Value

List with the following components:

consensus TOM only present if input return TOMs is TRUE. A list containing consensus TOM for

each block, stored as a distance structure.

TOMFiles only present if input saveConsensusTOMs is TRUE. A vector of file names, one

for each block, in which the TOM for the corresponding block is stored. TOM

is saved as a distance structure to save space.

saveConsensusTOMs

a copy of the input saveConsensusTOMs.

individualTOMInfo

information about individual set TOMs. A copy of the input individual TOMInfo

if given; otherwise the result of calling blockwiseIndividualTOMs. See blockwiseIndividualTOMs

for details.

Further components are retained for debugging and/or convenience.

useIndivTOMSubset

a copy of the input useIndivTOMSubset.

goodSamplesAndGenes

a list containing information about which samples and genes are "good" in the sense that they do not contain more than a certain fraction of missing data and (for genes) have non-zero variance. See goodSamplesGenesMS for details.

nGGenes number of "good" genes in goodSamplesGenes above.

nSets number of input sets.

saveCalibratedIndividualTOMs

a copy of the input saveCalibratedIndividualTOMs.

calibratedIndividualTOMFileNames

if input saveCalibratedIndividualTOMs is TRUE, this component will contain the file names of calibrated individual networks. The file names are arranged in a character matrix with each row corresponding to one input set and each

column to one block.

networkCalibrationSamples

if input getNetworkCalibrationSamples is TRUE, a list with one component per block. Each component is in turn a list with two components: sampleIndex is a vector contain the indices of the TOM samples (the indices refer to a flattened distance structure), and TOMSamples is a matrix of TOM samples with each row corresponding to a sample in sampleIndex, and each column to one input set.

consensusQuantile

a copy of the input consensusQuantile.

originCount A vector of length nSets that contains, for each set, the number of (calibrated)

elements that were less than or equal the consensus for that element.

Author(s)

118 consensusTreeInputs

References

WGCNA methodology has been described in

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17 PMID: 16646834

The original reference for the WGCNA package is

Langfelder P, Horvath S (2008) WGCNA: an R package for weighted correlation network analysis. BMC Bioinformatics 2008, 9:559 PMID: 19114008

For consensus modules, see

Langfelder P, Horvath S (2007) "Eigengene networks for studying the relationships between coexpression modules", BMC Systems Biology 2007, 1:54

This function uses quantile normalization described, for example, in

Bolstad BM1, Irizarry RA, Astrand M, Speed TP (2003) "A comparison of normalization methods for high density oligonucleotide array data based on variance and bias", Bioinformatics. 2003 Jan 22;19(2):1

See Also

blockwiseIndividualTOMs for calculation of topological overlaps across multiple sets.

consensus Tree Inputs

Get all elementary inputs in a consensus tree

Description

This function returns a flat vector or a structured list of elementary inputs to a given consensus tree, that is, inputs that are not consensus trees themselves.

Usage

consensusTreeInputs(consensusTree, flatten = TRUE)

Arguments

consensusTree A consensus tree of class ConsensusTree.

flatten Logical; if TRUE, the function returns a flat character vector of inputs; otherwise,

a list whose structure reflects the structure of consensusTree.

Value

A character vector of inputs or a list of inputs whose structure reflects the structure of consensusTree.

Author(s)

See Also

newConsensusTree for creating consensus trees.

convertNumericColumnsToNumeric

Convert character columns that represent numbers to numeric

Description

This function converts to numeric those character columns in the input that can be converted to numeric without generating missing values except for the allowed NA representations.

Usage

```
convertNumericColumnsToNumeric(
  data,
  naStrings = c("NA", "NULL", "NO DATA"),
  unFactor = TRUE)
```

Arguments

data A data frame.

naStrings Character vector of values that are allowd to convert to NA (a missing numeric

value).

unFactor Logical: should the function first convert all factor columns to character?

Value

A data frame with convertible columns converted to numeric.

Author(s)

120 cor

cor

Fast calculations of Pearson correlation.

Description

These functions implements a faster calculation of (weighted) Pearson correlation.

The speedup against the R's standard cor function will be substantial particularly if the input matrix only contains a small number of missing data. If there are no missing data, or the missing data are numerous, the speedup will be smaller.

Usage

```
cor(x, y = NULL,
    use = "all.obs",
    method = c("pearson", "kendall", "spearman"),
    weights.x = NULL,
    weights.y = NULL,
    quick = 0,
    cosine = FALSE,
    cosineX = cosine,
    cosineY = cosine,
    drop = FALSE,
    nThreads = 0,
    verbose = 0, indent = 0)
corFast(x, y = NULL,
    use = "all.obs",
    quick = 0, nThreads = 0,
    verbose = 0, indent = 0)
cor1(x, use = "all.obs", verbose = 0, indent = 0)
```

Arguments

X	a numeric vector or a matrix. If y is null, x must be a matrix.
У	a numeric vector or a matrix. If not given, correlations of columns of \boldsymbol{x} will be calculated.
use	a character string specifying the handling of missing data. The fast calculations currently support "all.obs" and "pairwise.complete.obs"; for other options, see R's standard correlation function cor. Abbreviations are allowed.
method	a character string specifying the method to be used. Fast calculations are currently available only for "pearson".
weights.x	optional observation weights for x. A matrix of the same dimensions as x, containing non-negative weights. Only used in fast calculations: methods must be "pearson" and use must be one of "all.obs", "pairwise.complete.obs".

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weights.y	optional observation weights for y. A matrix of the same dimensions as y, containing non-negative weights. Only used in fast calculations: methods must be "pearson" and use must be one of "all.obs", "pairwise.complete.obs".
quick	real number between 0 and 1 that controls the precision of handling of missing data in the calculation of correlations. See details.
cosine	logical: calculate cosine correlation? Only valid for method="pearson". Cosine correlation is similar to Pearson correlation but the mean subtraction is not performed. The result is the cosine of the angle(s) between (the columns of) x and y.
cosineX	logical: use the cosine calculation for x? This setting does not affect y and can be used to give a hybrid cosine-standard correlation.
cosineY	logical: use the cosine calculation for y? This setting does not affect x and can be used to give a hybrid cosine-standard correlation.
drop	logical: should the result be turned into a vector if it is effectively one-dimensional?
nThreads	non-negative integer specifying the number of parallel threads to be used by certain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads. Note that this option does not affect what is usually the most expensive part of the calculation, namely the matrix multiplication. The matrix multiplication is carried out by BLAS routines provided by R; these can be sped up by installing a fast BLAS and making R use it.
verbose	Controls the level of verbosity. Values above zero will cause a small amount of diagnostic messages to be printed.
indent	Indentation of printed diagnostic messages. Each unit above zero adds two spaces.

Details

The fast calculations are currently implemented only for method="pearson" and use either "all.obs" or "pairwise.complete.obs". The corFast function is a wrapper that calls the function cor. If the combination of method and use is implemented by the fast calculations, the fast code is executed; otherwise, R's own correlation cor is executed.

The argument quick specifies the precision of handling of missing data. Zero will cause all calculations to be executed precisely, which may be significantly slower than calculations without missing data. Progressively higher values will speed up the calculations but introduce progressively larger errors. Without missing data, all column means and variances can be pre-calculated before the covariances are calculated. When missing data are present, exact calculations require the column means and variances to be calculated for each covariance. The approximate calculation uses the pre-calculated mean and variance and simply ignores missing data in the covariance calculation. If the number of missing data is high, the pre-calculated means and variances may be very different from the actual ones, thus potentially introducing large errors. The quick value times the number of rows specifies the maximum difference in the number of missing entries for mean and variance calculations on the one hand and covariance on the other hand that will be tolerated before a recalculation is triggered. The hope is that if only a few missing data are treated approximately, the error introduced will be small but the potential speedup can be significant.

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Value

The matrix of the Pearson correlations of the columns of x with columns of y if y is given, and the correlations of the columns of x if y is not given.

Note

The implementation uses the BLAS library matrix multiplication function for the most expensive step of the calculation. Using a tuned, architecture-specific BLAS may significantly improve the performance of this function.

The values returned by the corFast function may differ from the values returned by R's function cor by rounding errors on the order of 1e-15.

Author(s)

Peter Langfelder

References

Peter Langfelder, Steve Horvath (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software, 46(11), 1-17. https://www.jstatsoft.org/v46/i11/

See Also

R's standard Pearson correlation function cor.

Examples

```
## Test the speedup compared to standard function cor
# Generate a random matrix with 200 rows and 1000 columns
set.seed(10)
nrow = 100;
ncol = 500;
data = matrix(rnorm(nrow*ncol), nrow, ncol);
## First test: no missing data
system.time( {corStd = stats::cor(data)} );
system.time( {corFast = cor(data)} );
all.equal(corStd, corFast)
# Here R's standard correlation performs very well.
# We now add a few missing entries.
data[sample(nrow, 10), 1] = NA;
```

corAndPvalue 123

```
# And test the correlations again...
system.time( {corStd = stats::cor(data, use ='p')} );
system.time( {corFast = cor(data, use = 'p')} );
all.equal(corStd, corFast)
# Here the R's standard correlation slows down considerably # while corFast still retains it speed. Choosing # higher ncol above will make the difference more pronounced.
```

corAndPvalue

Calculation of correlations and associated p-values

Description

A faster, one-step calculation of Student correlation p-values for multiple correlations, properly taking into account the actual number of observations.

Usage

Arguments

X	a vector or a matrix
у	a vector or a matrix. If NULL, the correlation of columns of \boldsymbol{x} will be calculated.
use	determines handling of missing data. See cor for details.
alternative	specifies the alternative hypothesis and must be (a unique abbreviation of) one of "two.sided", "greater" or "less". the initial letter. "greater" corresponds to positive association, "less" to negative association.
	other arguments to the function cor.

Details

The function calculates correlations of a matrix or of two matrices and the corresponding Student p-values. The output is not as full-featured as cor.test, but can work with matrices as input.

124 corPredictionSuccess

Value

A list with the following components, each a matrix:

cor the calculated correlations

p the Student p-values corresponding to the calculated correlations

Z Fisher transforms of the calculated correlationst Student t statistics of the calculated correlations

nObs Numbers of observations for the correlation, p-values etc.

Author(s)

Peter Langfelder and Steve Horvath

References

```
Peter Langfelder, Steve Horvath (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software, 46(11), 1-17. https://www.jstatsoft.org/v46/i11/
```

See Also

```
cor for calculation of correlations only;
cor.test for another function for significance test of correlations
```

Examples

```
# generate random data with non-zero correlation
set.seed(1);
a = rnorm(100);
b = rnorm(100) + a;
x = cbind(a, b);
# Call the function and display all results
corAndPvalue(x)
# Set some components to NA
x[c(1:4), 1] = NA
corAndPvalue(x)
# Note that changed number of observations.
```

corPredictionSuccess

Qunatification of success of gene screening

Description

This function calculates the success of gene screening.

Usage

```
corPredictionSuccess(corPrediction, corTestSet, topNumber = 100)
```

corPvalueFisher 125

Arguments

corPrediction a vector or a matrix of prediction statistics corTestSet correlation or other statistics on test set

topNumber a vector of the number of top genes to consider

Details

For each column in corPrediction, the function evaluates the mean corTestSet for the number of top genes (ranked by the column in corPrediction) given in topNumber. The higher the mean corTestSet (for positive corPrediction) or negative (for negative corPrediction), the more successful the prediction.

Value

meancorTestSetOverall

 $\label{thm:content} difference\ of\ mean corTestSetPositive\ and\ mean corTestSetNegative\ below\ mean corTestSetPositive$

mean corTestSet on top genes with positive corPrediction

meancorTestSetNegative

mean corTestSet on top genes with negative corPrediction

...

Author(s)

Steve Horvath

See Also

relativeCorPredictionSuccess

Description

Calculates Fisher's asymptotic p-value for given correlations.

Usage

```
corPvalueFisher(cor, nSamples, twoSided = TRUE)
```

Arguments

cor A vector of correlation values whose corresponding p-values are to be calculated

nSamples Number of samples from which the correlations were calculated

twoSided logical: should the calculated p-values be two sided?

126 correlationPreservation

Value

A vector of p-values of the same length as the input correlations.

Author(s)

Steve Horvath and Peter Langfelder

corPvalueStudent

Student asymptotic p-value for correlation

Description

Calculates Student asymptotic p-value for given correlations.

Usage

```
corPvalueStudent(cor, nSamples)
```

Arguments

cor A vector of correlation values whose corresponding p-values are to be calculated

nSamples Number of samples from which the correlations were calculated

Value

A vector of p-values of the same length as the input correlations.

Author(s)

Steve Horvath and Peter Langfelder

correlationPreservation

Preservation of eigengene correlations

Description

Calculates a summary measure of preservation of eigengene correlations across data sets

Usage

```
correlationPreservation(multiME, setLabels, excludeGrey = TRUE, greyLabel = "grey")
```

Arguments

multiME consensus module eigengenes in a multi-set format. A vector of lists with one

list corresponding to each set. Each list must contain a component data that is

a data frame whose columns are consensus module eigengenes.

setLabels names to be used for the sets represented in multiME.

excludeGrey logical: exclude the 'grey' eigengene from preservation measure?

greyLabel module label corresponding to the 'grey' module. Usually this will be the char-

acter string "grey" if the labels are colors, and the number 0 if the labels are

numeric.

Details

The function calculates the preservation of correlation of each eigengene with all other eigengenes (optionally except the 'grey' eigengene) in all pairs of sets.

Value

A data frame whose rows correspond to consensus module eigengenes given in the input multiME, and columns correspond to all possible set comparisons. The two sets compared in each column are indicated in the column name.

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

multiSetMEs and modulecheckSets in package moduleColor for more on eigengenes and the multi-set format

coxRegressionResiduals

Deviance- and martingale residuals from a Cox regression model

Description

The function inputs a censored time variable which is specified by two input variables time and event. It outputs i) the martingale residual and ii) deviance residual corresponding to a Cox regression model. By default, the Cox regression model is an intercept only Cox regression model. But optionally, the user can input covariates using the argument datCovariates. The function makes use of the coxph function in the survival library. See help(residuals.coxph) to learn more.

Usage

coxRegressionResiduals(time, event, datCovariates = NULL)

Arguments

time is a numeric variable that contains follow up time or time to event.

event is a binary variable that takes on values 1 and 0. 1 means that the event took

place (e.g. person died, or tumor recurred). 0 means censored, i.e. event has not

yet been observed or loss to follow up.

datCovariates a data frame whose columns correspond to covariates that should be used in the

Cox regression model. By default, the only covariate the intercept term 1.

Details

Residuals are often used to investigate the lack of fit of a model. For Cox regression, there is no easy analog to the usual "observed minus predicted" residual of linear regression. Instead, several specialized residuals have been proposed for Cox regression analysis. The function calculates residuals that are well defined for an intercept only Cox regression model: the martingale and deviance residuals (Therneau et al 1990). The martingale residual of a subject (person) specifies excess failures beyond the expected baseline hazard. For example, a subject who was censored at 3 years, and whose predicted cumulative hazard at 3 years was 30 Another subject who had an event at 10 years, and whose predicted cumulative hazard at 10 years was 60 Since martingale residuals are not symmetrically distributed, even when the fitted model is correct, it is often advantageous to transform them into more symmetrically distributed residuals: deviance residuals. Thus, deviance residuals are defined as transformations of the martingale residual and the event variable. Deviance residuals are often symmetrically distributed around zero Deviance Residuals are similar to residuals from ordinary linear regression in that they are symmetrically distributed around 0 and have standard deviation of 1.0. . A subjects with a large deviance residual is poorly predicted by the model, i.e. is different from the baseline cumulative hazard. A negative value indicates a longer than expected survival time. When covariates are specified in datCovariates, then one can plot deviance (or martingale) residuals against the covariates. Unusual patterns may indicate poor fit of the Cox model. Cryptic comments: Deviance (or martingale) residuals can sometimes be used as (uncensored) quantitative variables instead of the original time censored variable. For example, they could be used as outcome in a regression tree or regression forest predictor.

Value

It outputs a data frame with 2 columns. The first and second column correspond to martingale and deviance residuals respectively.

Note

This function can be considered a wrapper of the coxph function.

Author(s)

Steve Horvath

cutreeStatic 129

References

Thereneau TM, Grambsch PM, Fleming TR (1990) Martingale-based residuals for survival models. Biometrika (1990), 77, 1, pp. 147-60

Examples

```
library(survival)
# simulate time and event data
time1=sample(1:100)
event1=sample(c(1,0), 100,replace=TRUE)

event1[1:5]=NA
time1[1:5]=NA
# no covariates
datResiduals= coxRegressionResiduals(time=time1,event=event1)

# now we simulate a covariate
z= rnorm(100)
cor(datResiduals,use="p")
datResiduals=coxRegressionResiduals(time=time1,event=event1,datCovariates=data.frame(z))
cor(datResiduals,use="p")
```

cutreeStatic

Constant-height tree cut

Description

Module detection in hierarchical dendrograms using a constant-height tree cut. Only branches whose size is at least minSize are retained.

Usage

```
cutreeStatic(dendro, cutHeight = 0.9, minSize = 50)
```

Arguments

dendro a hierarchical clustering dendrogram such as returned by hclust.

cutHeight height at which branches are to be cut.

minSize minimum number of object on a branch to be considered a cluster.

Details

This function performs a straightforward constant-height cut as implemented by cutree, then calculates the number of objects on each branch and only keeps branches that have at least minSize objects on them.

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Value

A numeric vector giving labels of objects, with 0 meaning unassigned. The largest cluster is conventionally labeled 1, the next largest 2, etc.

Author(s)

Peter Langfelder

See Also

hclust for hierarchical clustering, cutree and cutreeStatic for other constant-height branch cuts, standardColors to convert the retuned numerical lables into colors for easier visualization.

cutreeStaticColor

Constant height tree cut using color labels

Description

Cluster detection by a constant height cut of a hierarchical clustering dendrogram.

Usage

```
cutreeStaticColor(dendro, cutHeight = 0.9, minSize = 50)
```

Arguments

dendro a hierarchical clustering dendrogram such as returned by hclust.

cutHeight height at which branches are to be cut.

minSize minimum number of object on a branch to be considered a cluster.

Details

This function performs a straightforward constant-height cut as implemented by cutree, then calculates the number of objects on each branch and only keeps branches that have at least minSize objects on them.

Value

A character vector giving color labels of objects, with "grey" meaning unassigned. The largest cluster is conventionally labeled "turquoise", next "blue" etc. Run standardColors() to see the sequence of standard color labels.

Author(s)

displayColors 131

See Also

hclust for hierarchical clustering, cutree and cutreeStatic for other constant-height branch cuts, standardColors to see the sequence of color labels that can be assigned.

displayColors

Show colors used to label modules

Description

The function plots a barplot using colors that label modules.

Usage

```
displayColors(colors = NULL)
```

Arguments

colors

colors to be displayed. Defaults to all colors available for module labeling.

Details

To see the first n colors, use argument colors = standardColors(n).

Value

None.

Author(s)

Peter Langfelder

See Also

standardColors

Examples

```
displayColors(standardColors(10))
```

dynamicMergeCut

dynamicMergeCut

Threshold for module merging

Description

Calculate a suitable threshold for module merging based on the number of samples and a desired Z quantile.

Usage

```
dynamicMergeCut(n, mergeCor = 0.9, Zquantile = 2.35)
```

Arguments

n number of samples

mergeCor theoretical correlation threshold for module merging

Zquantile Z quantile for module merging

Details

This function calculates the threshold for module merging. The threshold is calculated as the lower boundary of the interval around the theoretical correlation mergeCor whose width is given by the Z value Zquantile.

Value

The correlation threshold for module merging; a single number.

Author(s)

Steve Horvath

See Also

moduleEigengenes, mergeCloseModules

Examples

```
dynamicMergeCut(20)
dynamicMergeCut(50)
dynamicMergeCut(100)
```

empiricalBayesLM

Empirical Bayes-moderated adjustment for unwanted covariates

Description

This functions removes variation in high-dimensional data due to unwanted covariates while preserving variation due to retained covariates. To prevent numerical instability, it uses Empirical bayes-moderated linear regression, optionally in a robust (outlier-resistant) form.

Usage

```
empiricalBayesLM(
  data,
  removedCovariates,
  retainedCovariates = NULL,
  initialFitFunction = NULL,
  initialFitOptions = NULL,
  initialFitRequiresFormula = NULL,
  initialFit.returnWeightName = NULL,
  fitToSamples = NULL,
 weights = NULL,
  automaticWeights = c("none", "bicov"),
  aw.maxPOutliers = 0.1,
 weightType = c("apriori", "empirical"),
  stopOnSmallWeights = TRUE,
 minDesignDeviation = 1e-10,
  robustPriors = FALSE,
  tol = 1e-4, maxIterations = 1000,
  garbageCollectInterval = 50000,
  scaleMeanToSamples = fitToSamples,
  scaleMeanOfSamples = NULL,
  getOLSAdjustedData = TRUE,
  getResiduals = TRUE,
  getFittedValues = TRUE,
  getWeights = TRUE,
  getEBadjustedData = TRUE,
  verbose = 0, indent = 0)
```

Arguments

data

A 2-dimensional matrix or data frame of numeric data to be adjusted. Variables (for example, genes or methylation profiles) should be in columns and observations (samples) should be in rows.

removedCovariates

A vector or two-dimensional object (matrix or data frame) giving the covariates whose effect on the data is to be removed. At least one such covariate must be given.

retainedCovariates

A vector or two-dimensional object (matrix or data frame) giving the covariates whose effect on the data is to be retained. May be NULL if there are no such "retained" covariates.

initialFitFunction

Function name to perform the initial fit. The default is to use the internal implementation of linear model fitting. The function must take arguments formula and data or x and y, plus possibly additional arguments. The return value must be a list with component coefficients, either scale or residuals, and weights must be returned in component specified by initialFit.returnWeightName. See lm, rlm and other standard fit functions for examples of suitable functions.

initialFitOptions

Optional specifications of extra arguments for initialFitFunction, apart from formula and data or x and y. Defaults are provided for function rlm, i.e., if this function is used as initialFitFunction, suitable initial fit options will be chosen automatically.

initialFitRequiresFormula

Logical: does the initial fit function need formula and data arguments? If TRUE, initialFitFunction will be called with arguments formula and data, otherwise with arguments x and y.

initialFit.returnWeightName

Name of the component of the return value of initialFitFunction that contains the weights used in the fit. Suitable default value will be chosen automatically for rlm.

fitToSamples

Optional index of samples from which the linear model fits should be calculated. Defaults to all samples. If given, the models will be only fit to the specified samples but all samples will be transformed using the calculated coefficients.

weights

Optional 2-dimensional matrix or data frame of the same dimensions as data giving weights for each entry in data. These weights will be used in the initial fit and are are separate from the ones returned by initialFitFunction if it is specified.

automaticWeights

One of (unique abrreviations of) "none" or "bicov", instructing the function to calculate weights from the given data. Value "none" will result in trivial weights; value "bicov" will result in biweight midcovariance weights being used.

aw.maxPOutliers

If automaticWeights above is "bicov", this argument gets passed to the function bicovWeights and determines the maximum proportion of outliers in calculating the weights. See bicovWeights for more details.

weightType

One of (unique abbreviations of) "apriori" or "empirical". Determines whether a standard ("apriori") or a modified ("empirical") weighted regression is used. The "apriori" choice is suitable for weights that have been determined without knowledge of the actual data, while "empirical" is appropriate for situations where one wants to down-weigh cartain entries of data because they may be outliers. In either case, the weights should be determined in a way that is independent of the covariates (both retained and removed).

stopOnSmallWeights

Logical: should presence of small "apriori" weights trigger an error? Because standard weighted regression assumes that all weights are non-zero (otherwise estimates of standard errors will be biased), this function will by default complain about the presence of too small "apriori" weights.

minDesignDeviation

Minimum standard deviation for columns of the design matrix to be retained. Columns with standard deviations below this number will be removed (effectively removing the corresponding terms from the design).

robustPriors

Logical: should robust priors be used? This essentially means replacing mean by median and covariance by biweight mid-covariance.

tol

Convergence criterion used in the numerical equation solver. When the relative change in coefficients falls below this threshold, the system will be considered to have converged.

maxIterations

Maximum number of iterations to use.

garbageCollectInterval

Number of variables after which to call garbage collection.

scaleMeanToSamples

Optional specification of samples (given as a vector of indices) to whose means the resulting adjusted data should be scaled (more precisely, shifted).

scaleMeanOfSamples

Optional specification of samples (given as a vector of indices) that will be used in calculating the shift. Specifically, the shift is such that the mean of samples given in scaleMeanOfSamples will equal the mean of samples given in scaleMeanToSamples. Defaults to all samples.

getOLSAdjustedData

Logical: should data adjusted by ordinary least squares or by initialFitFunction, if specified, be returned?

getResiduals
getFittedValues

Logical: should the residuals (adjusted values without the means) be returned?

Logical: should fitted values be returned?

getWeights

Logical: should the final weights be returned?

getEBadjustedData

Logical: should the EB step be performed and the adjusted data returned? If this is FALSE, the function acts as a rather slow but still potentially useful adjustment using standard fit functions.

verbose Level of verbosity. Zero means silent, higher values result in more diagnostic

messages being printed.

indent Indentation of diagnostic messages. Each unit adds two spaces.

Details

This function uses Empirical Bayes-moderated (EB) linear regression to remove variation in data due to the variables in removedCovariates while retaining variation due to variables in retainedCovariates, if any are given. The EB step uses simple normal priors on the regression coefficients and inverse gamma priors on the variances. The procedure starts with multivariate ordinary linear regression of individual columns in data on retainedCovariates and removedCovariates. Alternatively, the user may specify an intial fit function (e.g., robust linear regression). To make the coefficients comparable, columns of data are scaled to (weighted if weights are given) mean 0 and variance 1. The resulting regression coefficients are used to determine the parameters of the normal prior (mean, covariance, and inverse gamma or median and biweight mid-covariance if robust priors are used), and the variances are used to determine the parameters of the inverse gamma prior. The EB step then essentially shrinks the coefficients toward their means, with the amount of shrinkage determined by the prior covariance.

Using appropriate weights can make the data adjustment robust to outliers. This can be achieved automatically by using the argument automaticWeights = "bicov". When bicov weights are used, we also recommend setting the argument maxPOutliers to a maximum proportion of samples that could be outliers. This is especially important if some of the design variables are binary and can be expected to have a strong effect on some of the columns in data, since standard biweight midcorrelation (and its weights) do not work well on bimodal data.

The automatic bicov weights are determined from data only. It is implicitly assumed that there are no outliers in the retained and removed covariates. Outliers in the covariates are more difficult to work with since, even if the regression is made robust to them, they can influence the adjusted values for the sample in which they appear. Unless the the covariate outliers can be attributed to a relevant variation in experimental conditions, samples with covariate outliers are best removed entirely before calling this function.

Value

A list with the following components (some of which may be missing depending on input options):

adjustedData A matrix of the same dimensions as the input data, giving the adjusted data. If

input data has non-NULL dimnames, these are copied.

residuals A matrix of the same dimensions as the input data, giving the residuals, that is,

adjusted data with zero means.

coefficients A matrix of regression coefficients. Rows correspond to the design matrix vari-

ables (mean, retained and removed covariates) and columns correspond to the

variables (columns) in data.

coefficiens.scaled

A matrix of regression coefficients corresponding to columns in data scaled to

mean 0 and variance 1.

sigmaSq Estimated error variances (one for each column of input data.

sigmaSq.scaled Estimated error variances corresponding to columns in data scaled to mean 0 and variance 1.

fittedValues Fitted values calculated from the means and coefficients corresponding to the removed covariates, i.e., roughly the values that are subtracted out of the data.

adjustedData.OLS

A matrix of the same dimensions as the input data, giving the data adjusted by ordinary least squares. This component should only be used for diagnostic purposes, not as input for further downstream analyses, as the OLS adjustment is inferior to EB adjustment.

residuals.OLS A matrix of the same dimensions as the input data, giving the residuals obtained from ordinary least squares regression, that is, OLS-adjusted data with zero means.

coefficients.OLS

A matrix of ordinary least squares regression coefficients. Rows correspond to the design matrix variables (mean, retained and removed covariates) and columns correspond to the variables (columns) in data.

coefficiens.OLS.scaled

A matrix of ordinary least squares regression coefficients corresponding to columns in data scaled to mean 0 and variance 1. These coefficients are used to calculate priors for the EB step.

sigmaSq.OLS Estimated OLS error variances (one for each column of input data.

sigmaSq.OLS.scaled

Estimated OLS error variances corresponding to columns in data scaled to mean 0 and variance 1. These are used to calculate variance priors for the EB step.

fittedValues.OLS

OLS fitted values calculated from the means and coefficients corresponding to the removed covariates.

weights A matrix of weights used in the regression models. The matrix has the same dimension as the input data.

dataColumnValid

Logical vector with one element per column of input data, indicating whether the column was adjusted. Columns with zero variance or too many missing data cannot be adjusted.

dataColumnWithZeroVariance

Logical vector with one element per column of input data, indicating whether the column had zero variance.

coefficientValid

Logical matrix of the dimension (number of covariates +1) times (number of variables in data), indicating whether the corresponding regression coefficient is valid. Invalid regression coefficients may be returned as missing values or as zeroes.

Author(s)

See Also

bicovWeights for suitable weights that make the adjustment robust to outliers.

```
exportNetworkToCytoscape
```

Export network to Cytoscape

Description

This function exports a network in edge and node list files in a format suitable for importing to Cytoscape.

Usage

```
exportNetworkToCytoscape(
   adjMat,
   edgeFile = NULL,
   nodeFile = NULL,
   weighted = TRUE,
   threshold = 0.5,
   nodeNames = NULL,
   altNodeNames = NULL,
   nodeAttr = NULL,
   includeColNames = TRUE)
```

Arguments

adjMat	adjacency matrix giving connection strengths among the nodes in the network.
edgeFile	file name of the file to contain the edge information.
nodeFile	file name of the file to contain the node information.

nodeFile file name of the file to contain the node information.

weighted logical: should the exported network be weighted?

threshold adjacency threshold for including edges in the output.

nodeNames names of the nodes. If not given, dimnames of adjMat will be used.

altNodeNames optional alternate names for the nodes, for example gene names if nodes are

labeled by probe IDs.

nodeAttr optional node attribute, for example module color. Can be a vector or a data

frame.

include ColNames

logical: should column names be included in the output files? Note that Cytoscape can read files both with and without column names.

Details

If the corresponding file names are supplied, the edge and node data is written to the appropriate files. The edge and node data is also returned as return value (see below).

Value

A list with the following componens:

egdeData a data frame containing the edge data, with one row per edge nodeData a data frame containing the node data, with one row per node

Author(s)

Peter Langfelder

See Also

exportNetworkToVisANT

exportNetworkToVisANT Export network data in format readable by VisANT

Description

Exports network data in a format readable and displayable by the VisANT software.

Usage

```
exportNetworkToVisANT(
  adjMat,
  file = NULL,
  weighted = TRUE,
  threshold = 0.5,
  maxNConnections = NULL,
  probeToGene = NULL)
```

Arguments

adjMat adjacency matrix of the network to be exported.

file character string specifying the file name of the file in which the data should be

written. If not given, no file will be created. The file is in a plain text format.

weighted logical: should the exported network by weighted? threshold adjacency threshold for including edges in the output.

maxNConnections

maximum number of exported adjacency edges. This can be used as another

filter on the exported edges.

probeToGene optional specification of a conversion between probe names (that label columns

and rows of adjacency) and gene names (that should label nodes in the output).

Details

The adjacency matrix is checked for validity. The entries can be negative, however. The adjacency matrix is expected to also have valid names or dimnames[[2]] that represent the probe names of the corresponding edges.

Whether the output is a weighted network or not, only edges whose (absolute value of) adjacency are above threshold will be included in the output. If maxNConnections is given, at most maxNConnections will be included in the output.

If probeToGene is given, it is expected to have two columns, the first one corresponding to the probe names, the second to their corresponding gene names that will be used in the output.

Value

A data frame containing the network information suitable as input to VisANT. The same data frame is also written into a file specified by file, if given.

Author(s)

Peter Langfelder

References

VisANT software is available from http://www.visantnet.org/visantnet.html/.

factorizeNonNumericColumns

Turn non-numeric columns into factors

Description

Given a data frame, this function turns non-numeric columns into factors.

Usage

factorizeNonNumericColumns(data)

Arguments

data

A data frame. Non-data frame inputs (e.g., a matrix) are coerced to a data frame.

Details

A column is considered numeric if its storage mode is numeric or if it is a character vector, it only contains character representations of numbers and possibly missing values encoded as "NA", "NULL", "NO DATA".

Value

The input data frame with non-numeric columns turned into factors.

fixDataStructure 141

Author(s)

Peter Langfelder

fixDataStructure

Put single-set data into a form useful for multiset calculations.

Description

Encapsulates single-set data in a wrapper that makes the data suitable for functions working on multiset data collections.

Usage

```
fixDataStructure(data, verbose = 0, indent = 0)
```

Arguments

data A dataframe, matrix or array with two dimensions to be encapsulated.

verbose Controls verbosity. 0 is silent.

indent Controls indentation of printed progress messages. 0 means no indentation,

every unit adds two spaces.

Details

For multiset calculations, many quantities (such as expression data, traits, module eigengenes etc) are presented by a common structure, a vector of lists (one list for each set) where each list has a component data that contains the actual (expression, trait, eigengene) data for the corresponding set in the form of a dataframe. This funtion creates a vector of lists of length 1 and fills the component data with the content of parameter data.

Value

As described above, input data in a format suitable for functions operating on multiset data collections.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

See Also

checkSets

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Examples

```
singleSetData = matrix(rnorm(100), 10,10);
encapsData = fixDataStructure(singleSetData);
length(encapsData)
names(encapsData[[1]])
dim(encapsData[[1]]$data)
all.equal(encapsData[[1]]$data, singleSetData);
```

formatLabels

Break long character strings into multiple lines

Description

This function attempts to break long character strings into multiple lines by replacing a given pattern by a newline character.

Usage

```
formatLabels(
   labels,
   maxCharPerLine = 14,
   maxWidth = NULL,
   maxLines = Inf,
   cex = 1,
   font = 1,
   split = " ",
   fixed = TRUE,
   newsplit = split,
   keepSplitAtEOL = TRUE,
   capitalMultiplier = 1.4,
   eol = "\n",
   ellipsis = "...")
```

Arguments

labels	Character strings to be formatted.
maxCharPerLine	Integer giving the maximum number of characters per line.
maxWidth	Maximum width in user coordinates. If given, overrides maxCharPerLine above and usually gives a much more efficient formatting.
maxLines	Maximum lines to retain. If a label extends past the maximum number of lines, ellipsis is added at the end of the last line.
cex	Character expansion factor that the user intends to use when adding labels to the current figure. Only used when maxWidth is specified.
font	Integer specifying the font. See par for details.

split Pattern to be replaced by newline ('\n') characters.

fixed Logical: Should the pattern be interpreted literally (TRUE) or as a regular expres-

sion (FALSE)? See strsplit and its argument fixed.

newsplit Character string to replace the occurrences of split above with.

keepSplitAtEOL When replacing an occurrence of split with a newline character, should the

newsplit be added before the newline as well?

capitalMultiplier

A multiplier for capital letters which typically occupy more space than lower-

case letters.

eol Character string to separate lines in the output.

ellipsis Character string to add to the last line if the input label is longer than fits on

maxLines lines.

Details

Each given element of labels is processed independently. The character string is split using strsplit, with split as the splitting pattern. The resulting shorter character strings are then concatenated together with newsplit as the separator. Whenever the length (adjusted using the capital letter multiplier) of the combined result from the start or the previous newline character exceeds maxCharPerLine, or strwidth exceeds maxWidth, the character specified by eol is inserted (at the previous split).

Note that individual segements (i.e., sections of the input between occurrences of split) whose number of characters exceeds maxCharPerLine will not be split.

Value

A character vector of the same length as input labels.

Author(s)

Peter Langfelder

Examples

```
s = "A quick hare jumps over the brown fox";
formatLabels(s);
```

fundamentalNetworkConcepts

Calculation of fundamental network concepts from an adjacency matrix.

Description

This function computes fundamental network concepts (also known as network indices or statistics) based on an adjacency matrix and optionally a node significance measure. These network concepts are defined for any symmetric adjacency matrix (weighted and unweighted). The network concepts are described in Dong and Horvath (2007) and Horvath and Dong (2008). Fundamental network concepts are defined as a function of the off-diagonal elements of an adjacency matrix adj and/or a node significance measure GS.

Usage

fundamentalNetworkConcepts(adj, GS = NULL)

Arguments

adj an adjacency matrix, that is a square, symmetric matrix with entries between 0

and 1

GS a node significance measure: a vector of the same length as the number of rows

(and columns) of the adjacency matrix.

Value

A list with the following components:

Connectivity a numerical vector that reports the connectivity (also known as degree) of each

node. This fundamental network concept is also known as whole network con-

nectivity. One can also define the scaled connectivity K=Connectivity/max(Connectivity)

which is used for computing the hub gene significance.

ScaledConnectivity

the Connectivity vector scaled by the highest connectivity in the network, i.e.,

Connectivity/max(Connectivity).

ClusterCoef a numerical vector that reports the cluster coefficient for each node. This funda-

mental network concept measures the cliquishness of each node.

MAR a numerical vector that reports the maximum adjacency ratio for each node.

MAR[i] equals 1 if all non-zero adjacencies between node i and the remaining network nodes equal 1. This fundamental network concept is always 1 for nodes of an unweighted network. This is a useful measure for weighted networks since it allows one to determine whether a node has high connectivity because of many weak connections (small MAR) or because of strong (but few) connections (high

MAR), see Horvath and Dong 2008.

Density the density of the network.

Centralization the centralization of the network.

Heterogeneity the heterogeneity of the network.

Author(s)

Steve Horvath

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

See Also

conformityBasedNetworkConcepts for calculation of conformity based network concepts for a network adjacency matrix;

networkConcepts, for calculation of conformity based and eigennode based network concepts for a correlation network.

GOenrichmentAnalysis

Calculation of GO enrichment (experimental)

Description

NOTE: GOenrichmentAnalysis is deprecated. Please use function enrichmentAnalysis from R package anRichment, available from https://labs.genetics.ucla.edu/horvath/htdocs/CoexpressionNetwork/GeneAnnotation/

WARNING: This function should be considered experimental. The arguments and resulting values (in particular, the enrichment p-values) are not yet finalized and may change in the future. The function should only be used to get a quick and rough overview of GO enrichment in the modules in a data set; for a publication-quality analysis, please use an established tool.

Using Bioconductor's annotation packages, this function calculates enrichments and returns terms with best enrichment values.

Usage

Arguments

labels cluster (module, group) labels of genes to be analyzed. Either a single vector, or

a matrix. In the matrix case, each column will be analyzed separately; analyzing a collection of module assignments in one function call will be faster than calling the function several tinmes. For each row, the labels in all columns must

correspond to the same gene specified in entrezCodes.

entrezCodes Entrez (a.k.a. LocusLink) codes of the genes whose labels are given in labels.

A single vector; the i-th entry corresponds to row i of the matrix labels (or to

the i-the entry if labels is a vector).

yeastORFs if organism=="yeast" (below), this argument can be used to input yeast open

reading frame (ORF) identifiers instead of Entrez codes. Since the GO mappings for yeast are provided in terms of ORF identifiers, this may lead to a more accurate GO enrichment analysis. If given, the argument entrezCodes is ig-

nored.

organism character string specifying the organism for which to perform the analysis. Rec-

ognized values are (unique abbreviations of) "human", "mouse", "rat", "malaria",

"yeast", "fly", "bovine", "worm", "canine", "zebrafish", "chicken".

ontologies vector of character strings specifying GO ontologies to be included in the anal-

ysis. Can be any subset of "BP", "CC", "MF". The result will contain the terms with highest enrichment in each specified category, plus a separate list of terms

with best enrichment in all ontologies combined.

evidence vector of character strings specifying admissible evidence for each gene in its

specific term, or "all" for all evidence codes. See Details or http://www.geneontology.org/GO.evidence.shi

for available evidence codes and their meaning.

includeOffspring

logical: should genes belonging to the offspring of each term be included in the term? As a default, only genes belonging directly to each term are associated with the term. Note that the calculation of enrichments with offspring included

can be quite slow for large data sets.

backgroundType specification of the background to use. Recognized values are (unique abbre-

viations of) "allGiven", "allInGO", "givenInGO", meaning that the functions will take all genes given in labels as backround ("allGiven"), all genes present in any of the GO categories ("allInGO"), or the intersection of given genes and genes present in GO ("givenInGO"). The default is recommended

for genome-wide enrichment studies.

removeDuplicates

logical: should duplicate entries in entrezCodes be removed? If TRUE, only the first occurence of each unique Entrez code will be kept. The cluster labels

labels will be adjusted accordingly.

leaveOutLabel optional specifications of module labels for which enrichment calculation is not

desired. Can be a single label or a vector of labels to be ignored. However, if in any of the sets no labels are left to calculate enrichment of, the function will

stop with an error.

nBestP specifies the number of terms with highest enrichment whose detailed informa-

tion will be returned.

pCut alternative specification of terms to be returned: all terms whose enrichment p-

value is more significant than pCut will be returned. If pCut is given, nBestP is

ignored.

nBiggest in addition to returning terms with highest enrichment, terms that contain most

of the genes in each cluster can be returned by specifying the number of biggest terms per cluster to be returned. This may be useful for development and testing

purposes.

getTermDetails logical indicating whether detailed information on the most enriched terms should

be returned.

verbose integer specifying the verbosity of the function. Zero means silent, positive

values will cause the function to print progress reports.

indent integer specifying indentation of the diagnostic messages. Zero means no in-

dentation, each unit adds two spaces.

Details

This function is basically a wrapper for the annotation packages available from Bioconductor. It requires the packages GO.db, AnnotationDbi, and org.xx.eg.db, where xx is the code corresponding to the organism that the user wishes to analyze (e.g., Hs for human Homo Sapiens, Mm for mouse Mus Musculus etc). For each cluster specified in the input, the function calculates all enrichments in the specified ontologies, and collects information about the terms with highest enrichment. The enrichment p-value is calculated using Fisher exact test. As background we use all of the supplied genes that are present in at least one term in GO (in any of the ontologies).

For best results, the newest annotation libraries should be used. Because of the way Bioconductor is set up, to get the newest annotation libraries you may have to use the current version of R.

According to http://www.geneontology.org/GO.evidence.shtml, the following codes are used by GO:

Experimental Evidence Codes

EXP: Inferred from Experiment

IDA: Inferred from Direct Assay

IPI: Inferred from Physical Interaction

IMP: Inferred from Mutant Phenotype

IGI: Inferred from Genetic Interaction

IEP: Inferred from Expression Pattern

Computational Analysis Evidence Codes

ISS: Inferred from Sequence or Structural Similarity

ISO: Inferred from Sequence Orthology

ISA: Inferred from Sequence Alignment

ISM: Inferred from Sequence Model

IGC: Inferred from Genomic Context

IBA: Inferred from Biological aspect of Ancestor

IBD: Inferred from Biological aspect of Descendant

IKR: Inferred from Key Residues

IRD: Inferred from Rapid Divergence

RCA: inferred from Reviewed Computational Analysis

Author Statement Evidence Codes
TAS: Traceable Author Statement
NAS: Non-traceable Author Statement

Curator Statement Evidence Codes

IC: Inferred by Curator

ND: No biological Data available

Automatically-assigned Evidence Codes

IEA: Inferred from Electronic Annotation

Obsolete Evidence Codes NR: Not Recorded

Value

A list with the following components:

keptForAnalysis

logical vector with one entry per given gene. TRUE if the entry was used for enrichment analysis. Depending on the setting of removeDuplicates above, only a single entry per gene may be used.

inG0

logical vector with one entry per given gene. TRUE if the gene belongs to any GO term, FALSE otherwise. Also FALSE for genes not used for the analysis because of duplication.

If input labels contained only one vector of labels, the following components:

countsInTerms a matrix whose rows correspond to given cluster, and whose columns correspond

to GO terms, contaning number of genes in the intersection of the corresponding

module and GO term. Row and column names are set appropriately.

enrichmentP a matrix whose rows correspond to given cluster, and whose columns correspond

to GO terms, contaning enrichment p-values of each term in each cluster. Row

and column names are set appropriately.

bestPTerms a list of lists with each inner list corresponding to an ontology given in ontologies

in input, plus one component corresponding to all given ontologies combined. The name of each component is set appropriately. Each inner list contains two components: enrichment is a data frame containing the highest enriched terms for each module; and forModule is a list of lists with one inner list per module, appropriately named. Each inner list contains one component per term. If input getTermDeyails is TRUE, this component is yet another list and contains components termName (term name), enrichmentP (enrichment P value), termDefinition (GO term definition), termOntology (GO term ontology), geneCodes (Entrez codes of module genes in this term), genePositions (indices of the genes listed in geneCodes within the given labels). Thus, to obtain information on say the second term of the 5th module in ontology BP, one can look at the appropriate row of bestPTerms\$BP\$enrichment, or one can

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reference bestPTerms\$BP\$forModule[[5]][[2]]. The author of the function apologizes for any confusion this structure of the output may cause.

biggestTerms

a list of the same format as bestPTerms, containing information about the terms with most genes in the module for each supplied ontology.

If input labels contained more than one vector, instead of the above components the return value contains a list named setResults that has one component per given set; each component is a list containing the above components for the corresponding set.

Author(s)

Peter Langfelder

See Also

Bioconductor's annotation packages such as GO.db and organism-specific annotation packages such as org.Hs.eg.db.

goodGenes

Filter genes with too many missing entries

Description

This function checks data for missing entries and returns a list of genes that have non-zero variance and pass two criteria on maximum number of missing values and values whose weight is below a threshold: the fraction of missing values must be below a given threshold and the total number of present samples must be at least equal to a given threshold. If weights are given, entries whose relative weight is below a threshold will be considered missing.

Usage

```
goodGenes(
  datExpr,
  weights = NULL,
  useSamples = NULL,
  useGenes = NULL,
  minFraction = 1/2,
  minNSamples = ..minNSamples,
  minNGenes = ..minNGenes,
  tol = NULL,
  minRelativeWeight = 0.1,
  verbose = 1, indent = 0)
```

goodGenes goodGenes

Arguments

useGenes

datExpr expression data. A data frame in which columns are genes and rows ar samples.

weights optional observation weights in the same format (and dimensions) as datExpr.

optional specifications of which samples to use for the check. Should be a logical vector; samples whose entries are FALSE will be ignored for the missing value counts. Defaults to using all samples.

optional specifications of genes for which to perform the check. Should be a

logical vector; genes whose entries are FALSE will be ignored. Defaults to using

all genes.

minFraction minimum fraction of non-missing samples for a gene to be considered good.
minNSamples minimum number of non-missing samples for a gene to be considered good.
minNGenes minimum number of good genes for the data set to be considered fit for analysis.

If the actual number of good genes falls below this threshold, an error will be

issued.

tol an optional 'small' number to compare the variance against. Defaults to the

square of 1e-10 * max(abs(datExpr), na.rm = TRUE). The reason of comparing the variance to this number, rather than zero, is that the fast way of computing variance used by this function sometimes causes small numerical overflow errors which make variance of constant vectors slightly non-zero; comparing the variance to tol rather than zero prevents the retaining of such genes as 'good

genes'.

minRelativeWeight

observations whose relative weight is below this threshold will be considered missing. Here relative weight is weight divided by the maximum weight in the

column (gene).

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The constants ..minNSamples and ..minNGenes are both set to the value 4.

If weights are given, entries whose relative weight (i.e., weight divided by maximum weight in the column or gene) will be considered missing.

For most data sets, the fraction of missing samples criterion will be much more stringent than the absolute number of missing samples criterion.

Value

A logical vector with one entry per gene that is TRUE if the gene is considered good and FALSE otherwise. Note that all genes excluded by useGenes are automatically assigned FALSE.

Author(s)

Peter Langfelder and Steve Horvath

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See Also

goodSamples, goodSamplesGenes

goodGenesMS

Filter genes with too many missing entries across multiple sets

Description

This function checks data for missing entries and returns a list of genes that have non-zero variance in all sets and pass two criteria on maximum number of missing values in each given set: the fraction of missing values must be below a given threshold and the total number of missing samples must be below a given threshold. If weights are given, entries whose relative weight is below a threshold will be considered missing.

Usage

```
goodGenesMS(
  multiExpr,
  multiWeights = NULL,
  useSamples = NULL,
  useGenes = NULL,
  minFraction = 1/2,
  minNSamples = ..minNSamples,
  minNGenes = ..minNGenes,
  tol = NULL,
  minRelativeWeight = 0.1,
  verbose = 1, indent = 0)
```

Arguments

multiExpr	expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.
multiWeights	optional observation weights in the same format (and dimensions) as $\verb multiExpr .$
useSamples	optional specifications of which samples to use for the check. Should be a logical vector; samples whose entries are FALSE will be ignored for the missing value counts. Defaults to using all samples.
useGenes	optional specifications of genes for which to perform the check. Should be a logical vector; genes whose entries are FALSE will be ignored. Defaults to using all genes.
minFraction	minimum fraction of non-missing samples for a gene to be considered good.
minNSamples	minimum number of non-missing samples for a gene to be considered good.

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minNGenes minimum number of good genes for the data set to be considered fit for analysis.

If the actual number of good genes falls below this threshold, an error will be

issued.

tol an optional 'small' number to compare the variance against. For each set in

multiExpr, the default value is 1e-10 * max(abs(multiExpr[[set]]\$data), na.rm = TRUE). The reason of comparing the variance to this number, rather than zero, is that the fast way of computing variance used by this function sometimes causes small numerical overflow errors which make variance of constant vectors slightly non-zero; comparing the variance to tol rather than zero prevents the

retaining of such genes as 'good genes'.

minRelativeWeight

observations whose relative weight is below this threshold will be considered

missing. Here relative weight is weight divided by the maximum weight in the

column (gene).

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The constants ..minNSamples and ..minNGenes are both set to the value 4.

If weights are given, entries whose relative weight (i.e., weight divided by maximum weight in the column or gene) will be considered missing.

For most data sets, the fraction of missing samples criterion will be much more stringent than the absolute number of missing samples criterion.

Value

A logical vector with one entry per gene that is TRUE if the gene is considered good and FALSE otherwise. Note that all genes excluded by useGenes are automatically assigned FALSE.

Author(s)

Peter Langfelder

See Also

goodGenes, goodSamples, goodSamplesGenes for cleaning individual sets separately; goodSamplesMS, goodSamplesGenesMS for additional cleaning of multiple data sets together.

goodSamples 153

goodSamples	Filter samples with too many missing entries

Description

This function checks data for missing entries and returns a list of samples that pass two criteria on maximum number of missing values: the fraction of missing values must be below a given threshold and the total number of missing genes must be below a given threshold.

Usage

```
goodSamples(
  datExpr,
  weights = NULL,
  useSamples = NULL,
  useGenes = NULL,
  minFraction = 1/2,
  minNSamples = ..minNSamples,
  minNGenes = ..minNGenes,
  minRelativeWeight = 0.1,
  verbose = 1, indent = 0)
```

Arguments

datExpr	expression data. A data frame in which columns are genes and rows ar samples.	
weights	optional observation weights in the same format (and dimensions) as datExpr.	
useSamples	optional specifications of which samples to use for the check. Should be a logical vector; samples whose entries are FALSE will be ignored for the missing value counts. Defaults to using all samples.	
useGenes	optional specifications of genes for which to perform the check. Should be a logical vector; genes whose entries are FALSE will be ignored. Defaults to using all genes.	
minFraction	minimum fraction of non-missing samples for a gene to be considered good.	
minNSamples	minimum number of good samples for the data set to be considered fit for analysis. If the actual number of good samples falls below this threshold, an error will be issued.	
minNGenes	minimum number of non-missing samples for a sample to be considered good.	
minRelativeWeight		
	observations whose weight divided by the maximum weight is below this threshold will be considered missing.	
verbose	integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.	
indent	indentation for diagnostic messages. Zero means no indentation, each unit adds two spaces.	

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Details

The constants ..minNSamples and ..minNGenes are both set to the value 4. For most data sets, the fraction of missing samples criterion will be much more stringent than the absolute number of missing samples criterion.

Value

A logical vector with one entry per sample that is TRUE if the sample is considered good and FALSE otherwise. Note that all samples excluded by useSamples are automatically assigned FALSE.

Author(s)

Peter Langfelder and Steve Horvath

See Also

```
goodSamples, goodSamplesGenes
```

goodSamplesGenes

Iterative filtering of samples and genes with too many missing entries

Description

This function checks data for missing entries, entries with weights below a threshold, and zero-variance genes, and returns a list of samples and genes that pass criteria on maximum number of missing or low weight values. If necessary, the filtering is iterated.

Usage

```
goodSamplesGenes(
  datExpr,
  weights = NULL,
  minFraction = 1/2,
  minNSamples = ..minNSamples,
  minNGenes = ..minNGenes,
  tol = NULL,
  minRelativeWeight = 0.1,
  verbose = 1, indent = 0)
```

Arguments

datExpr	expression data. A matrix or data frame in which columns are genes and rows ar samples.
weights	optional observation weights in the same format (and dimensions) as datExpr.
minFraction	minimum fraction of non-missing samples for a gene to be considered good.
minNSamples	minimum number of non-missing samples for a gene to be considered good.

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minNGenes minimum number of good genes for the data set to be considered fit for analysis.

If the actual number of good genes falls below this threshold, an error will be

issued.

tol an optional 'small' number to compare the variance against. Defaults to the

square of 1e-10 * max(abs(datExpr), na.rm = TRUE). The reason of comparing the variance to this number, rather than zero, is that the fast way of computing variance used by this function sometimes causes small numerical overflow errors which make variance of constant vectors slightly non-zero; comparing the variance to tol rather than zero prevents the retaining of such genes as 'good

genes'.

minRelativeWeight

observations whose relative weight is below this threshold will be considered

missing. Here relative weight is weight divided by the maximum weight in the

column (gene).

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function iteratively identifies samples and genes with too many missing entries and genes with zero variance. If weights are given, entries with relative weight (weight divided by maximum weight in the column) below minRelativeWeight will be considered missing. The process is repeated until the lists of good samples and genes are stable. The constants ..minNSamples and ..minNGenes are both set to the value 4.

Value

A list with the foolowing components:

goodSamples A logical vector with one entry per sample that is TRUE if the sample is consid-

ered good and FALSE otherwise.

goodGenes A logical vector with one entry per gene that is TRUE if the gene is considered

good and FALSE otherwise.

Author(s)

Peter Langfelder

See Also

goodSamples, goodGenes

goodSamplesGenesMS

Iterative filtering of samples and genes with too many missing entries across multiple data sets

Description

This function checks data for missing entries and zero variance across multiple data sets and returns a list of samples and genes that pass criteria maximum number of missing values. If weights are given, entries whose relative weight is below a threshold will be considered missing. The filtering is iterated until convergence.

Usage

```
goodSamplesGenesMS(
  multiExpr,
  multiWeights = NULL,
  minFraction = 1/2,
  minNSamples = ..minNSamples,
  minNGenes = ..minNGenes,
  tol = NULL,
  minRelativeWeight = 0.1,
  verbose = 2, indent = 0)
```

Arguments

multiExpr

expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights

 $optional\ observation\ weights\ in\ the\ same\ format\ (and\ dimensions)\ as\ {\tt multiExpr}.$

minFraction minNSamples

minimum fraction of non-missing samples for a gene to be considered good. minimum number of non-missing samples for a gene to be considered good.

minNGenes

minimum number of good genes for the data set to be considered fit for analysis. If the actual number of good genes falls below this threshold, an error will be

issued

tol

an optional 'small' number to compare the variance against. For each set in multiExpr, the default value is 1e-10 * max(abs(multiExpr[[set]]\$data), na.rm = TRUE). The reason of comparing the variance to this number, rather than zero, is that the fast way of computing variance used by this function sometimes causes small numerical overflow errors which make variance of constant vectors slightly non-zero; comparing the variance to tol rather than zero prevents the retaining of such genes as 'good genes'.

minRelativeWeight

observations whose relative weight is below this threshold will be considered missing. Here relative weight is weight divided by the maximum weight in the column (gene).

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verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function iteratively identifies samples and genes with too many missing entries, and genes with zero variance; iterations are necessary since excluding samples effectively changes criteria on genes and vice versa. The process is repeated until the lists of good samples and genes are stable. If weights are given, entries whose relative weight (i.e., weight divided by maximum weight in the column or gene) is below a threshold will be considered missing. The constants ..minNSamples and ..minNGenes are both set to the value 4.

Value

A list with the foolowing components:

goodSamples A list with one component per given set. Each component is a logical vector

with one entry per sample in the corresponding set that is TRUE if the sample is

considered good and FALSE otherwise.

goodGenes A logical vector with one entry per gene that is TRUE if the gene is considered

good and FALSE otherwise.

Author(s)

Peter Langfelder

See Also

goodGenes, goodSamples, goodSamplesGenes for cleaning individual sets separately; goodSamplesMS, goodGenesMS for additional cleaning of multiple data sets together.

goodSamplesMS

Filter samples with too many missing entries across multiple data sets

Description

This function checks data for missing entries and returns a list of samples that pass two criteria on maximum number of missing values: the fraction of missing values must be below a given threshold and the total number of missing genes must be below a given threshold.

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Usage

```
goodSamplesMS(multiExpr,
    multiWeights = NULL,
    useSamples = NULL,
    useGenes = NULL,
    minFraction = 1/2,
    minNSamples = ..minNSamples,
    minNGenes = ..minNGenes,
    minRelativeWeight = 0.1,
    verbose = 1, indent = 0)
```

Arguments

multiExpr expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression

data, with rows corresponding to samples and columns to genes or probes.

multiWeights optional observation weights in the same format (and dimensions) as multiExpr.

useSamples optional specifications of which samples to use for the check. Should be a log-

ical vector; samples whose entries are FALSE will be ignored for the missing

value counts. Defaults to using all samples.

useGenes optional specifications of genes for which to perform the check. Should be a

logical vector; genes whose entries are FALSE will be ignored. Defaults to using

all genes.

minFraction minimum fraction of non-missing samples for a gene to be considered good.

minNSamples minimum number of good samples for the data set to be considered fit for anal-

ysis. If the actual number of good samples falls below this threshold, an error

will be issued.

minNGenes minimum number of non-missing samples for a sample to be considered good.

minRelativeWeight

observations whose relative weight is below this threshold will be considered missing. Here relative weight is weight divided by the maximum weight in the

column (gene).

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The constants ..minNSamples and ..minNGenes are both set to the value 4.

If weights are given, entries whose relative weight (i.e., weight divided by maximum weight in the column or gene) will be considered missing.

For most data sets, the fraction of missing samples criterion will be much more stringent than the absolute number of missing samples criterion.

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Value

A list with one component per input set. Each component is a logical vector with one entry per sample in the corresponding set, indicating whether the sample passed the missing value criteria.

Author(s)

Peter Langfelder and Steve Horvath

See Also

goodGenes, goodSamples, goodSamplesGenes for cleaning individual sets separately; goodGenesMS, goodSamplesGenesMS for additional cleaning of multiple data sets together.

greenBlackRed

Green-black-red color sequence

Description

Generate a green-black-red color sequence of a given length.

Usage

```
greenBlackRed(n, gamma = 1)
```

Arguments

n number of colors to be returned

gamma color correction power

Details

The function returns a color vector that starts with pure green, gradually turns into black and then to red. The power gamma can be used to control the behaviour of the quarter- and three quarter-values (between green and black, and black and red, respectively). Higher powers will make the mid-colors more green and red, respectively.

Value

A vector of colors of length n.

Author(s)

Peter Langfelder

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Examples

```
par(mfrow = c(3, 1))
displayColors(greenBlackRed(50));
displayColors(greenBlackRed(50, 2));
displayColors(greenBlackRed(50, 0.5));
```

greenWhiteRed

Green-white-red color sequence

Description

Generate a green-white-red color sequence of a given length.

Usage

```
greenWhiteRed(n, gamma = 1, warn = TRUE)
```

Arguments

n number of colors to be returned

gamma color change power

warn logical: should the user be warned that this function produces a palette unsuit-

able for people with most common color blindness?

Details

The function returns a color vector that starts with green, gradually turns into white and then to red. The power gamma can be used to control the behaviour of the quarter- and three quarter-values (between green and white, and white and red, respectively). Higher powers will make the mid-colors more white, while lower powers will make the colors more saturated, respectively.

Typical use of this function is to produce (via function numbers2colors) a color representation of numbers within a symmetric interval around 0, for example, the interval [-1, 1]. Note though that since green and red are not distinguishable by people with the most common type of color blindness, we recommend using the analogous palette returned by the function blueWhiteRed.

Value

A vector of colors of length n.

Author(s)

Peter Langfelder

See Also

blueWhiteRed for a color sequence more friendly to people with the most common type of color blindness;

numbers2colors for a function that produces a color representation for continuous numbers.

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Examples

```
par(mfrow = c(3, 1))
displayColors(greenWhiteRed(50));
title("gamma = 1")
displayColors(greenWhiteRed(50, 3));
title("gamma = 3")
displayColors(greenWhiteRed(50, 0.5));
title("gamma = 0.5")
```

 ${\sf GTOMdist}$

Generalized Topological Overlap Measure

Description

Generalized Topological Overlap Measure, taking into account interactions of higher degree.

Usage

```
GTOMdist(adjMat, degree = 1)
```

Arguments

adjMat adjacency matrix. See details below.

degree integer specifying the maximum degree to be calculated.

Value

Matrix of the same dimension as the input adjMat.

Author(s)

Steve Horvath and Andy Yip

References

Yip A, Horvath S (2007) Gene network interconnectedness and the generalized topological overlap measure. BMC Bioinformatics 2007, 8:22

hierarchicalConsensusCalculation

Hierarchical consensus calculation

Description

Hierarchical consensus calculation with optional data calibration.

Usage

```
hierarchicalConsensusCalculation(
   individualData,
   consensusTree,
   level = 1,
   useBlocks = NULL,
   randomSeed = NULL,
   saveCalibratedIndividualData = FALSE,
   calibratedIndividualDataFilePattern =
         "calibratedIndividualData-%a-Set%s-Block%b.RData",
   # Return options: the data can be either saved or returned but not both.
   saveConsensusData = TRUE,
   consensusDataFileNames = "consensusData-%a-Block%b.RData",
   getCalibrationSamples= FALSE,
   # Return the intermediate results as well?
   keepIntermediateResults = FALSE,
   # Internal handling of data
   useDiskCache = NULL,
   chunkSize = NULL,
   cacheDir = ".",
   cacheBase = ".blockConsModsCache",
   # Behaviour
   collectGarbage = FALSE,
   verbose = 1, indent = 0)
```

Arguments

individualData Individual data from which the consensus is to be calculated. It can be either a list or a multiData structure. Each element in individulData can in turn either be a numeric object (vector, matrix or array) or a BlockwiseData structure.

consensusTree A list specifying the consensus calculation. See details.

level Integer which the user should leave at 1. This serves to keep default set names

unique.

useBlocks When individualData contains BlockwiseData, this argument can be an inte-

ger vector with indices of blocks for which the calculation should be performed.

randomSeed If non-NULL, the function will save the current state of the random generator, set

the given seed, and restore the random seed to its original state upon exit. If

NULL, the seed is not set nor is it restored on exit.

saveCalibratedIndividualData

Logical: should calibrated individual data be saved?

calibrated Individual Data File Pattern

Pattern from which file names for saving calibrated individual data are determined. The conversions %a, %s and %b will be replaced by analysis name, set

number and block number, respectively.

saveConsensusData

Logical: should final consensus be saved (TRUE) or returned in the return value (FALSE)?

consensusDataFileNames

Pattern from which file names for saving the final consensus are determined. The conversions %a and %b will be replaced by analysis name and block number, respectively.

getCalibrationSamples

When calibration method in the consensusOptions component of ConsensusTree is "single quantile", this logical argument determines whether the calibration samples should be returned within the return value.

keepIntermediateResults

Logical: should results of intermediate consensus calculations (if any) be kept? These are always returned as BlockwiseData whose data are saved to disk.

useDiskCache

Logical: should disk cache be used for consensus calculations? The disk cache can be used to store chunks of calibrated data that are small enough to fit one chunk from each set into memory (blocks may be small enough to fit one block of one set into memory, but not small enough to fit one block from all sets in a consensus calculation into memory at the same time). Using disk cache is slower but lessens the memory footprint of the calculation. As a general guide, if individual data are split into blocks, we recommend setting this argument to TRUE. If this argument is NULL, the function will decide whether to use disk cache based on the number of sets and block sizes.

chunkSize Integer giving the chunk size. If left NULL, a suitable size will be chosen auto-

matically.

cacheDir Directory in which to save cache files. The files are deleted on normal exit but

persist if the function terminates abnormally.

cacheBase Base for the file names of cache files.

collectGarbage Logical: should garbage collection be forced after each major calculation?

verbose Integer level of verbosity of diagnostic messages. Zero means silent, higher

values make the output progressively more and more verbose.

indent Indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function calculates consensus in a hierarchical manner, using a separate (and possibly different) set of consensus options at each step. The "recipe" for the consensus calculation is supplied in the argument consensusTree.

The argument consensusTree should have the following components: (1) inputs must be either a character vector whose components match names(inputData), or consensus trees in the own right. (2) consensusOptions must be a list of class "ConsensusOptions" that specifies options for calculating the consensus. A suitable set of options can be obtained by calling newConsensusOptions. (3) Optionally, the component analysisName can be a single character string giving the name for the analysis. When intermediate results are returned, they are returned in a list whose names will be set from analysisName components, if they exist.

The actual consensus calculation at each level of the consensus tree is carried out in function consensusCalculation. The consensus options for each individual consensus calculation are independent from one another, i.e., the consensus options for different steps can be different.

Value

A list containing the output of the top level call to consensusCalculation; if keepIntermediateResults is TRUE, component inputs contains a (possibly recursive) list of the results of intermediate consensus calculations. Names of the inputs list are taken from the corresponding analysisName components if they exist, otherwise from names of the corresponding inputs components of the supplied consensusTree. See example below for an example of a relatively simple consensus tree.

Author(s)

Peter Langfelder

See Also

newConsensusOptions for obtaining a suitable list of consensus options; consensusCalculation for the actual calculation of a consensus that underpins this function.

Examples

hierarchicalConsensusKME 165

hierarchicalConsensusKME

Calculation of measures of fuzzy module membership (KME) in hierarchical consensus modules

Description

This function calculates several measures of fuzzy module membership in hiearchical consensus modules.

Usage

```
hierarchicalConsensusKME(
   multiExpr,
   moduleLabels,
   multiWeights = NULL,
   multiEigengenes = NULL,
   consensusTree,
   signed = TRUE,
   useModules = NULL,
   metaAnalysisWeights = NULL,
   corAndPvalueFnc = corAndPvalue, corOptions = list(),
   corComponent = "cor", getFDR = FALSE,
   useRankPvalue = TRUE,
   rankPvalueOptions = list(calculateQvalue = getFDR, pValueMethod = "scale"),
   setNames = names(multiExpr), excludeGrey = TRUE,
   greyLabel = if (is.numeric(moduleLabels)) 0 else "grey",
   reportWeightType = NULL,
   getOwnModuleZ = TRUE,
   getBestModuleZ = TRUE,
   getOwnConsensusKME = TRUE,
   getBestConsensusKME = TRUE,
   getAverageKME = FALSE,
   getConsensusKME = TRUE,
```

```
getMetaColsFor1Set = FALSE,
getMetaP = FALSE,
getMetaFDR = getMetaP && getFDR,

getSetKME = TRUE,
getSetZ = FALSE,
getSetP = FALSE,
getSetPDR = getSetP && getFDR,

includeID = TRUE,
additionalGeneInfo = NULL,
includeWeightTypeInColnames = TRUE)
```

Arguments

multiExpr Expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

moduleLabels A vector with one entry per column (gene or probe) in multiExpr, giving the

module labels.

multiWeights optional observation weights for data in multiExpr, in the same format (and

dimensions) as multiExpr. These weights are used in calculation of KME, i.e., the correlation of module eigengenes with data in multiExpr. The module

eigengenes are not weighted in this calculation.

multiEigengenes

Optional specification of module eigengenes of the modules (module Labels) in

data sets within multiExpr. If not given, will be calculated.

consensusTree A list specifying the consensus calculation. See details.

signed Logical: should module membership be considered singed? Signed member-

ship should be used for signed (including signed hybrid) networks and means that negative module membership means the gene is not a member of the module. In other words, in signed networks negative kME values are not considered significant and the corresponding p-values will be one-sided. In unsigned networks, negative kME values are considered significant and the corresponding

p-values will be two-sided.

useModules Optional vector specifying which modules should be used. Defaults to all mod-

ules except the unassigned module.

metaAnalysisWeights

Optional specification of meta-analysis weights for each input set. If given, must be a numeric vector of length equal the number of input data sets (i.e., length(multiExpr)). These weights will be used in addition to constant weights and weights proportional to number of samples (observations) in each set.

corAndPvalueFnc

Function that calculates associations between expression profiles and eigengenes. See details.

corOptions List giving additional arguments to function corAndPvalueFnc. See details.

corComponent Name of the component of output of corAndPvalueFnc that contains the actual

correlation.

getFDR Logical: should FDR be calculated?

useRankPvalue Logical: should the rankPvalue function be used to obtain alternative meta-

analysis statistics?

rankPvalueOptions

Additional options for function rankPvalue. These include na.last (default "keep"), ties.method (default "average"), calculateQvalue (default copied from input getQvalues), and pValueMethod (default "scale"). See the help

file for rankPvalue for full details.

setNames Names for the input sets. If not given, will be taken from names(multiExpr).

If those are NULL as well, the names will be "Set_1", "Set_2",

excludeGrey logical: should the grey module be excluded from the kME tables? Since the

grey module is typically not a real module, it makes little sense to report kME

values for it.

greyLabel label that labels the grey module.

reportWeightType

One of "equal", "rootDoF", "DoF", "user". Indicates which of the weights should be reported in the output. If not given, all available weight types will be reported; this always includes "equal", "rootDoF", "DoF", while "user"

weights are reported if metaAnalysisWeights above is given.

getOwnModuleZ Logical: should meta-analysis Z statistic in own module be returned as a column

of the output?

getBestModuleZ Logical: should highest meta-analysis Z statistic across all modules and the

corresponding module be returned as columns of the output?

getOwnConsensusKME

Logical: should consensus KME (eigengene-based connectivity) statistic in own

module be returned as a column of the output?

getBestConsensusKME

Logical: should highest consensus KME across all modules and the correspond-

ing module be returned as columns of the output?

getAverageKME Logical: Should average KME be calculated?

getConsensusKME

Logical: should consensus KME be calculated?

getMetaColsFor1Set

Logical: should the meta-statistics be returned if the input data only have 1

set? For 1 set, meta- and individual kME values are the same, so meta-columns

essentially duplicate individual columns.

getMetaP Logical: should meta-analysis p-values corresponding to the KME meta-analysis

Z statistics be calculated?

getMetaFDR Logical: should FDR estimates for the meta-analysis p-values corresponding to

the KME meta-analysis Z statistics be calculated?

getSetKME Logical: should KME values for individual sets be returned?

getSetZ Logical: should Z statistics corresponding to KME for individual sets be re-

turned?

getSetP Logical: should p values corresponding to KME for individual sets be returned?

getSetFDR Logical: should FDR estimates corresponding to KME for individual sets be

returned?

includeID Logical: should gene ID (taken from column names of multiExpr) be included

as the first column in the output?

additionalGeneInfo

Optional data frame with rows corresponding to genes in multiExpr that should

be included as part of the output.

includeWeightTypeInColnames

Logical: should weight type ("equal", "rootDoF", "DoF", "user") be in-

cluded in appropriate meta-analysis column names?

Details

This function calculates several measures of (hierarchical) consensus KME (eigengene-based intramodular connectivity or fuzzy module membership) for all genes in all modules.

First, it calculates the meta-analysis Z statistics for correlations between genes and module eigengenes; this is known as the consensus module membership Z statistic. The meta-analysis weights can be specified by the user either explicitly or implicitly ("equal", "RootDoF" or "DoF").

Second, it can calculate the consensus KME, i.e., the hierarchical consensus of the KMEs (correlations with eigengenes) across the individual sets. The consensus calculation is specified in the argument consensusTree; typically, the consensusTree used here will be the same as the one used for the actual consensus network construction and module identification. See newConsensusTree for details on how to specify consensus trees.

Third, the function can also calculate the (weighted) average KME using the meta-analysis weights; the average KME can be interpreted as the meta-analysis of the KMEs in the individual sets. This is related to but somewhat distinct from the meta-analysis Z statistics.

In addition to these, optional output also includes, for each gene, KME values in the module to which the gene is assigned as well as the maximum KME values and modules for which the maxima are attained. For most genes, the assigned module will be the one with highest KME values, but for some genes the assigned module and module of maximum KME may be different.

The function corAndPvalueFnc is currently is expected to accept arguments x (gene expression profiles), y (eigengene expression profiles), and alternative with possibilities at least "greater", "two.sided". If weights are given, these are passed to corAndPvalueFnc as argument weights.x. Any additional arguments can be passed via corOptions.

The function corAndPvalueFnc should return a list which at the least contains (1) a matrix of associations of genes and eigengenes (this component should have the name given by corComponent), and (2) a matrix of the corresponding p-values, named "p" or "p.value". Other components are optional but for full functionality should include (3) n0bs giving the number of observations for each association (which is the number of samples less number of missing data - this can in principle vary from association to association), and (4) Z giving a Z static for each observation. If these are missing, n0bs is calculated in the main function, and calculations using the Z statistic are skipped.

Value

Data frame with the following components, some of which may be missing depending on input options (for easier readability the order here is not the same as in the actual output):

ID Gene ID, taken from the column names of the first input data set

If given, a copy of additionalGeneInfo.

Z.kME.inOwnModule

Meta-analysis Z statistic for membership in assigned module.

maxZ.kME Maximum meta-analysis Z statistic for membership across all modules.

moduleOfMaxZ.kME

Module in which the maximum meta-analysis Z statistic is attained.

consKME.inOwnModule

Consensus KME in assigned module.

 $\begin{tabular}{ll} maxConsKME & Maximum consensus KME across all modules. \\ moduleOfMaxConsKME & \begin{tabular}{ll} modules. \\ modu$

Module in which the maximum consensus KME is attained.

consensus.kME.1, consensus.kME.2, ...

Consensus kME (that is, the requested quantile of the kMEs in the individual data sets)in each module for each gene across the input data sets. The module labels (here 1, 2, etc.) correspond to those in moduleLabels.

weighted Average.equal Weights.k ME1, weighted Average.equal Weights.k ME2,

. . .

 $Average~kME~in~each~module~for~each~gene~across~the~input~data~sets.\\ weighted Average~.~RootDoFWeights~.~kME1,~weighted Average~.~RootDoFWeights~.~kME2,$

Weighted average kME in each module for each gene across the input data sets. The weight of each data set is proportional to the square root of the number of samples in the set.

 $weighted {\tt Average.DoFWeights.kME1}, \qquad weighted {\tt Average.DoFWeights.kME2},$

. . .

Weighted average kME in each module for each gene across the input data sets. The weight of each data set is proportional to number of samples in the set.

weightedAverage.userWeights.kME1, weightedAverage.userWeights.kME2,

. . .

(Only present if input metaAnalysisWeights is non-NULL.) Weighted average kME in each module for each gene across the input data sets. The weight of each data set is given in metaAnalysisWeights.

 ${\tt meta.Z.equalWeights.kME1, meta.Z.equalWeights.kME2, \dots}$

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set equally. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.Z.RootDoFWeights.kME1, meta.Z.RootDoFWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by the square root of the number of samples. Only returned if the function <code>corAndPvalueFnc</code> returns the Z statistics corresponding to the correlations.

meta.Z.DoFWeights.kME1, meta.Z.DoFWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by the number of samples. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.Z.userWeights.kME1, meta.Z.userWeights.kME2, ...

Meta-analysis Z statistic for kME in each module, obtained by weighing the Z scores in each set by metaAnalysisWeights. Only returned if metaAnalysisWeights is non-NULL and the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.p.equalWeights.kME1, meta.p.equalWeights.kME2, ...

p-values obtained from the equal-weight meta-analysis Z statistics. Only returned if the function <code>corAndPvalueFnc</code> returns the Z statistics corresponding to the correlations.

meta.p.RootDoFWeights.kME1, meta.p.RootDoFWeights.kME2, ...

p-values obtained from the meta-analysis Z statistics with weights proportional to the square root of the number of samples. Only returned if the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.p.DoFWeights.kME1, meta.p.DoFWeights.kME2, ...

p-values obtained from the degree-of-freedom weight meta-analysis Z statistics. Only returned if the function <code>corAndPvalueFnc</code> returns the Z statistics corresponding to the correlations.

meta.p.userWeights.kME1, meta.p.userWeights.kME2, ...

p-values obtained from the user-supplied weight meta-analysis Z statistics. Only returned if metaAnalysisWeights is non-NULL and the function corAndPvalueFnc returns the Z statistics corresponding to the correlations.

meta.q.equalWeights.kME1, meta.q.equalWeights.kME2, ...

q-values obtained from the equal-weight meta-analysis p-values. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.RootDoFWeights.kME1, meta.q.RootDoFWeights.kME2, ...

q-values obtained from the meta-analysis p-values with weights proportional to the square root of the number of samples. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.DoFWeights.kME1, meta.q.DoFWeights.kME2, ...

q-values obtained from the degree-of-freedom weight meta-analysis p-values. Only present if getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

meta.q.userWeights.kME1, meta.q.userWeights.kME2, ...

q-values obtained from the user-specified weight meta-analysis p-values. Only present if metaAnalysisWeights is non-NULL, getQvalues is TRUE and the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.

The next set of columns contain the results of function rankPvalue and are only present if input useRankPvalue is TRUE. Some columns may be missing depending on the options specified in rankPvalueOptions. We explicitly list columns that are based on weighing each set equally; names of these columns carry the suffix .equalWeights

pValueExtremeRank.ME1.equalWeights,pValueExtremeRank.ME2.equalWeights, This is the minimum between pValueLowRank and pValueHighRank, i.e. min(pValueLow, pValueHigh) pValueLowRank.ME1.equalWeights, pValueLowRank.ME2.equalWeights, ... Asymptotic p-value for observing a consistently low value based on the rank method. pValueHighRank.ME1.equalWeights, pValueHighRank.ME2.equalWeights, Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method. pValueExtremeScale.ME1.equalWeights, pValueExtremeScale.ME2.equalWeights, This is the minimum between pValueLowScale and pValueHighScale, i.e. min(pValueLow, pValueHigh) pValueLowScale.ME1.equalWeights, pValueLowScale.ME2.equalWeights, Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method. pValueHighScale.ME1.equalWeights, pValueHighScale.ME2.equalWeights, Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method. qValueExtremeRank.ME1.equalWeights,qValueExtremeRank.ME2.equalWeights, local false discovery rate (q-value) corresponding to the p-value pValueExtremeRqValueLowRank.ME1.equalWeights,qValueLowRank.ME2.equalWeights,... local false discovery rate (q-value) corresponding to the p-value pValueLowRank qValueHighRank.ME1.equalWeights, lueHighRank.ME2.equalWeights, ... local false discovery rate (q-value) corresponding to the p-value pValueHigh-Rank qValueExtremeScale.ME1.equalWeights,qValueExtremeScale.ME2.equalWeights, local false discovery rate (q-value) corresponding to the p-value pValueExtremeScale qValueLowScale.ME2.equalWeights, qValueLowScale.ME1.equalWeights, local false discovery rate (q-value) corresponding to the p-value pValueLowScale qValueHighScale.ME1.equalWeights, qValueHighScale.ME2.equalWeights, local false discovery rate (q-value) corresponding to the p-value pValueHigh-Analogous columns corresponding to weighing individual sets by the square root of the number of samples, by number of samples, and by user weights (if given). The corresponding column name suffixes are .RootDoFWeights, .DoFWeights, and .userWeights.

The following set of columns summarize kME in individual input data sets.

```
kME1.Set_1, kME1.Set_2, ..., kME2.Set_1, kME2.Set_2, ...

kME values for each gene in each module in each given data set.

p.kME1.Set_1, p.kME1.Set_2, ..., p.kME2.Set_1, p.kME2.Set_2, ...

p-values corresponding to kME values for each gene in each module in each given data set.

q.kME1.Set_1, q.kME1.Set_2, ..., q.kME2.Set_1, q.kME2.Set_2, ...

q-values corresponding to kME values for each gene in each module in each given data set. Only returned if getQvalues is TRUE.

Z.kME1.Set_1, Z.kME1.Set_2, ..., Z.kME2.Set_1, Z.kME2.Set_2, ...

Z statistics corresponding to kME values for each gene in each module in each given data set. Only present if the function corAndPvalueFnc returns the Z statistics corresponding to the kME values.
```

Author(s)

Peter Langfelder

See Also

signedKME for eigengene based connectivity in a single data set. corAndPvalue, bicorAndPvalue for two alternatives for calculating correlations and the corresponding p-values and Z scores. Both can be used with this function. newConsensusTree for more details on hierarchical consensus trees and calculations.

hierarchicalConsensusMEDissimilarity

Hierarchical consensus calculation of module eigengene dissimilarity

Description

Hierarchical consensus calculation of module eigengene dissimilarities, or more generally, correlation-based dissimilarities of sets of vectors.

Usage

```
hierarchicalConsensusMEDissimilarity(
   MEs,
   networkOptions,
   consensusTree,
   greyName = "ME0",
   calibrate = FALSE)
```

Arguments

MEs A multiData structure containing vectors (usually module eigengenes) whose

consensus dissimilarity is to be calculated.

networkOptions A multiData structure containing, for each input data set, a list of class NetworkOptions

giving options for network calculation for all of the networks.

consensusTree A list specifying the consensus calculation. See details.

greyName Name of the "grey" module eigengene. Currently not used.

calibrate Logical: should the dissimilarities be calibrated using the calibration method

specified in consensusTree? See details.

Details

This function first calculates the similarities of the ME vectors from their correlations, using the appropriate options in networkOptions (correlation type and options, signed or unsigned dissimilarity etc). This results in a similarity matrix in each of the input data sets.

Next, a hierarchical consensus of the similarities is calculated via a call to hierarchicalConsensusCalculation, using the consensus specification and options in consensusTree. In typical use, consensusTree contains the same consensus specification as the consensus network calculation that gave rise to the consensus modules whose eigengenes are contained in MEs but this is not mandatory.

The argument consensusTree should have the following components: (1) inputs must be either a character vector whose components match names(inputData), or consensus trees in the own right. (2) consensusOptions must be a list of class "ConsensusOptions" that specifies options for calculating the consensus. A suitable set of options can be obtained by calling newConsensusOptions. (3) Optionally, the component analysisName can be a single character string giving the name for the analysis. When intermediate results are returned, they are returned in a list whose names will be set from analysisName components, if they exist.

In the final step, the consensus similarity is turned into a dissimilarity by subtracting it from 1.

Value

A matrix with rows and columns corresponding to the variables (modules) in MEs, containing the consensus dissimilarities.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusCalculation for the actual consensus calculation.

hierarchicalConsensusModules

Hierarchical consensus network construction and module identifica-

Description

Hierarchical consensus network construction and module identification across multiple data sets.

Usage

```
hierarchicalConsensusModules(
   multiExpr,
   multiWeights = NULL,
   multiExpr.imputed = NULL,
   # Data checking options
   checkMissingData = TRUE,
   # Blocking options
   blocks = NULL,
   maxBlockSize = 5000,
   blockSizePenaltyPower = 5,
   nPreclusteringCenters = NULL,
   randomSeed = 12345,
   # Network construction options.
   networkOptions,
   # Save individual TOMs?
   saveIndividualTOMs = TRUE,
   individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",
   keepIndividualTOMs = FALSE,
   # Consensus calculation options
   consensusTree = NULL,
   # Return options
   saveConsensusTOM = TRUE,
   consensusTOMFilePattern = "consensusTOM-%a-Block%b.RData",
   # Keep the consensus?
   keepConsensusTOM = saveConsensusTOM,
   # Internal handling of TOMs
   useDiskCache = NULL, chunkSize = NULL,
   cacheBase = ".blockConsModsCache",
```

```
cacheDir = ".",
# Alternative consensus TOM input from a previous calculation
consensusTOMInfo = NULL,
# Basic tree cut options
deepSplit = 2,
detectCutHeight = 0.995, minModuleSize = 20,
checkMinModuleSize = TRUE,
# Advanced tree cut opyions
maxCoreScatter = NULL, minGap = NULL,
maxAbsCoreScatter = NULL, minAbsGap = NULL,
minSplitHeight = NULL, minAbsSplitHeight = NULL,
useBranchEigennodeDissim = FALSE,
minBranchEigennodeDissim = mergeCutHeight,
stabilityLabels = NULL,
stabilityCriterion = c("Individual fraction", "Common fraction"),
minStabilityDissim = NULL,
pamStage = TRUE, pamRespectsDendro = TRUE,
iteratePruningAndMerging = FALSE,
minCoreKME = 0.5, minCoreKMESize = minModuleSize/3,
minKMEtoStay = 0.2,
# Module eigengene calculation options
impute = TRUE,
trapErrors = FALSE,
excludeGrey = FALSE,
# Module merging options
calibrateMergingSimilarities = FALSE,
mergeCutHeight = 0.15,
# General options
collectGarbage = TRUE,
verbose = 2, indent = 0,
...)
```

Arguments

multiExpr

Expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights optional observation weights in the same format (and dimensions) as multiExpr. These weights are used for correlation calculations with data in multiExpr.

multiExpr.imputed

If multiExpr contain missing data, this argument can be used to supply the expression data with missing data imputed. If not given, the impute knn function will be used to impute the missing data.

checkMissingData

Logical: should data be checked for excessive numbers of missing entries in genes and samples, and for genes with zero variance? See details.

Optional specification of blocks in which hierarchical clustering and module detection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the corresponding gene belongs.

Integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not exceed maxBlockSize.

Number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block

size is very important.

Number of centers to be used in the preclustering. Defaults to smaller of nGenes/20 and 100*nGenes/maxBlockSize, where nGenes is the number of genes (variables) in multiExpr.

Integer to be used as seed for the random number generator before the function starts. If a current seed exists, it is saved and restored upon exit. If NULL is given, the function will not save and restore the seed.

networkOptions A single list of class NetworkOptions giving options for network calculation for all of the networks, or a multiData structure containing one such list for each input data set.

saveIndividualTOMs

Logical: should individual TOMs be saved to disk (TRUE) or retuned directly in the return value (FALSE)?

individualTOMFileNames

Character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

keepIndividualTOMs

Logical: should individual TOMs be retained after the calculation is finished?

consensusTree A list specifying the consensus calculation. See details. saveConsensusTOM

Logical: should the consensus TOM be saved to disk?

blocks

maxBlockSize

blockSizePenaltyPower

nPreclusteringCenters

randomSeed

consensusTOMFilePattern

Character string giving the file names to save consensus TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

keepConsensusTOM

Logical: should consensus TOM be retained after the calculation ends? Depending on saveConsensusTOM, the retained TOM is either saved to disk or returned within the return value.

useDiskCache

Logical: should disk cache be used for consensus calculations? The disk cache can be used to store chunks of calibrated data that are small enough to fit one chunk from each set into memory (blocks may be small enough to fit one block of one set into memory, but not small enough to fit one block from all sets in a consensus calculation into memory at the same time). Using disk cache is slower but lessens the memory footprint of the calculation. As a general guide, if individual data are split into blocks, we recommend setting this argument to TRUE. If this argument is NULL, the function will decide whether to use disk cache based on the number of sets and block sizes.

chunkSize

Integer giving the chunk size. If left NULL, a suitable size will be chosen automatically.

cacheDir

Directory in which to save cache files. The files are deleted on normal exit but persist if the function terminates abnormally.

cacheBase

Base for the file names of cache files.

consensusTOMInfo

If the consensus TOM has been pre-calculated using function hierarchicalConsensusTOM, this argument can be used to supply it. If given, the consensus TOM calculation options above are ignored.

deepSplit

Numeric value between 0 and 4. Provides a simplified control over how sensitive module detection should be to module splitting, with 0 least and 4 most sensitive. See cutreeDynamic for more details.

detectCutHeight

Dendrogram cut height for module detection. See cutreeDynamic for more details.

minModuleSize

Minimum module size for module detection. See cutreeDynamic for more de-

checkMinModuleSize

logical: should sanity checks be performed on minModuleSize?

maxCoreScatter maximum scatter of the core for a branch to be a cluster, given as the fraction of cutHeight relative to the 5th percentile of joining heights. See cutreeDynamic for more details.

minGap

minimum cluster gap given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. See cutreeDynamic for more details.

maxAbsCoreScatter

maximum scatter of the core for a branch to be a cluster given as absolute heights. If given, overrides maxCoreScatter. See cutreeDynamic for more details.

minAbsGap

minimum cluster gap given as absolute height difference. If given, overrides minGap. See cutreeDynamic for more details.

minSplitHeight Minimum split height given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. Branches merging below this height will automatically be merged. Defaults to zero but is used only if minAbsSplitHeight below is NULL.

minAbsSplitHeight

Minimum split height given as an absolute height. Branches merging below this height will automatically be merged. If not given (default), will be determined from minSplitHeight above.

useBranchEigennodeDissim

Logical: should branch eigennode (eigengene) dissimilarity be considered when merging branches in Dynamic Tree Cut?

minBranchEigennodeDissim

Minimum consensus branch eigennode (eigengene) dissimilarity for branches to be considerd separate. The branch eigennode dissimilarity in individual sets is simly 1-correlation of the eigennodes; the consensus is defined as quantile with probability consensusQuantile.

stabilityLabels

Optional matrix of cluster labels that are to be used for calculating branch dissimilarity based on split stability. The number of rows must equal the number of genes in multiExpr; the number of columns (clusterings) is arbitrary. See branchSplitFromStabilityLabels for details.

stabilityCriterion

One of c("Individual fraction", "Common fraction"), indicating which method for assessing stability similarity of two branches should be used. We recommend "Individual fraction" which appears to perform better; the "Common fraction" method is provided for backward compatibility since it was the (only) method available prior to WGCNA version 1.60.

minStabilityDissim

Minimum stability dissimilarity criterion for two branches to be considered separate. Should be a number between 0 (essentially no dissimilarity required) and 1 (perfect dissimilarity or distinguishability based on stabilityLabels). See branchSplitFromStabilityLabels for details.

pamStage

logical. If TRUE, the second (PAM-like) stage of module detection will be performed. See cutreeDynamic for more details.

pamRespectsDendro

Logical, only used when pamStage is TRUE. If TRUE, the PAM stage will respect the dendrogram in the sense an object can be PAM-assigned only to clusters that lie below it on the branch that the object is merged into. See cutreeDynamic for more details.

iteratePruningAndMerging

Logical: should pruning of low-KME genes and module merging be iterated? For backward compatibility, the default is FALSE but it setting it to TRUE may

lead to better-defined modules.

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize

genes with eigengene connectivity at least minCoreKME, the module is disbanded (its genes are unlabeled and returned to the pool of genes waiting for mofule de-

tection).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose eigengene connectivity to their module eigengene is lower than

minKMEtoStay are removed from the module.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

excludeGrey logical: should the returned module eigengenes exclude the eigengene of the

"module" that contains unassigned genes?

calibrateMergingSimilarities

Logical: should module eigengene similarities be calibrated before calculating the consensus? Although calibration is in principle desirable, the calibration methods currently available assume large data and do not work very well on

eigengene similarities.

mergeCutHeight Dendrogram cut height for module merging.

collectGarbage Logical: should garbage be collected after some of the memory-intensive steps?

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

... Other arguments. Currently ignored.

Details

This function calculates a consensus network with a flexible, possibly hierarchical consensus specification, identifies (consensus) modules in the network, and calculates their eigengenes. "Blockwise" calculation is available for large data sets for which a full network (TOM or adjacency matrix) would not fit into available RAM.

The input can be either several numerical data sets (expression etc) in the argument multiExpr together with all necessary network construction options, or a pre-calculated network, typically the result of a call to hierarchicalConsensusTOM.

Steps in the network construction include the following: (1) optional filtering of variables (genes) and observations (samples) that contain too many missing values or have zero variance; (2) optional pre-clustering to split data into blocks of manageable size; (3) calculation of adjacencies and optionally of TOMs in each individual data set; (4) calculation of consensus network from the individual networks; (5) hierarchical clustering and module identification; (6) trimming of modules by removing genes with low correlation with the eigengene of the module; and (7) merging of modules whose eigengenes are strongly correlated.

Steps 1-4 (up to and including the calculation of consensus network from the individual networks) are handled by the function hierarchicalConsensusTOM.

Variables (genes) are clustered using average-linkage hierarchical clustering and modules are identified in the resulting dendrogram by the Dynamic Hybrid tree cut.

Found modules are trimmed of genes whose consensus module membership kME (that is, correlation with module eigengene) is less than minKMEtoStay. Modules in which fewer than minCoreKMESize genes have consensus KME higher than minCoreKME are disbanded, i.e., their constituent genes are pronounced unassigned.

After all blocks have been processed, the function checks whether there are genes whose KME in the module they assigned is lower than KME to another module. If p-values of the higher correlations are smaller than those of the native module by the factor reassignThresholdPS (in every set), the gene is re-assigned to the closer module.

In the last step, modules whose eigengenes are highly correlated are merged. This is achieved by clustering module eigengenes using the dissimilarity given by one minus their correlation, cutting the dendrogram at the height mergeCutHeight and merging all modules on each branch. The process is iterated until no modules are merged. See mergeCloseModules for more details on module merging.

The module trimming and merging process is optionally iterated. Iterations are recommended but are (for now) not the default for backward compatibility.

Value

List with the following components:

labels	A numeric vector with one component per variable (gene), giving the module la-
	bel of each variable (gene). Label 0 is reserved for unassigned variables; module

labels are sequential and smaller numbers are used for larger modules.

unmergedLabels A numeric vector with one component per variable (gene), giving the unmerged

module label of each variable (gene), i.e., module labels before the call to mod-

ule merging.

colors A character vector with one component per variable (gene), giving the module

colors. The labels are mapped to colors using labels2colors.

unmergedColors A character vector with one component per variable (gene), giving the unmerged

module colors.

multiMEs Module eigengenes corresponding to the modules returned in colors, in multi-

set format. A vector of lists, one per set, containing eigengenes, proportion of variance explained and other information. See multiSetMEs for a detailed

description.

dendrograms A list with one component for each block of genes. Each component is the

hierarchical clustering dendrogram obtained by clustering the consensus gene

dissimilarity in the corresponding block.

consensusTOMInfo

A list detailing various aspects of the consensus TOM. See hierarchicalConsensusTOM for details.

blockInfo

A list with information about blocks as well as the vriables and observations (genes and samples) retained after filtering out those with zero variance and too many missing values.

moduleIdentificationArguments

A list with the module identification arguments supplied to this function. Contains deepSplit, detectCutHeight, minModuleSize, maxCoreScatter, minGap, maxAbsCoreScatter, minAbsGap, minSplitHeight, useBranchEigennodeDissim, minBranchEigennodeDissim, minStabilityDissim, pamStage, pamRespectsDendro, minCoreKME, minCoreKMESize, minKMEtoStay, calibrateMergingSimilarities, and mergeCutHeight.

Note

If the input datasets have large numbers of genes, consider carefully the maxBlockSize as it significantly affects the memory footprint (and whether the function will fail with a memory allocation error). From a theoretical point of view it is advantageous to use blocks as large as possible; on the other hand, using smaller blocks is substantially faster and often the only way to work with large numbers of genes. As a rough guide, when 4GB of memory are available, blocks should be no larger than 8,000 genes; with 8GB one can handle some 13,000 genes; with 16GB around 20,000; and with 32GB around 30,000. Depending on the operating system and its setup, these numbers may vary substantially.

Author(s)

Peter Langfelder

References

Non-hierarchical consensus networks are described in Langfelder P, Horvath S (2007), Eigengene networks for studying the relationships between co-expression modules. BMC Systems Biology 2007, 1:54.

 $More in-depth \ discussion \ of \ selected \ topics \ can \ be \ found \ at \ http://www.peterlangfelder.com/\ , \ and \ an \ FAQ \ at \ https://labs.genetics.ucla.edu/horvath/CoexpressionNetwork/Rpackages/WGCNA/faq.html$

See Also

hierarchicalConsensusTOM for calculation of hierarchical consensus networks (adjacency and TOM), and a more detailed description of the calculation;

hclust and cutreeHybrid for hierarchical clustering and the Dynamic Tree Cut branch cutting method;

mergeCloseModules for module merging;

blockwiseModules for an analogous analysis on a single data set.

hierarchicalConsensusTOM

Calculation of hierarchical consensus topological overlap matrix

Description

This function calculates consensus topological overlap in a hierarchical manner.

Usage

```
hierarchicalConsensusTOM(
      # ... information needed to calculate individual TOMs
      multiExpr,
      multiWeights = NULL,
      # Data checking options
      checkMissingData = TRUE,
      # Blocking options
      blocks = NULL,
      maxBlockSize = 20000,
      blockSizePenaltyPower = 5,
      nPreclusteringCenters = NULL,
      randomSeed = 12345,
      # Network construction options
      networkOptions,
      # Save individual TOMs?
      keepIndividualTOMs = TRUE,
      individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",
      \# ... or information about individual (more precisely, input) TOMs
      individualTOMInfo = NULL,
      # Consensus calculation options
      consensusTree,
      useBlocks = NULL,
      # Save calibrated TOMs?
      saveCalibratedIndividualTOMs = FALSE,
    calibratedIndividualTOMFilePattern = "calibratedIndividualTOM-Set%s-Block%b.RData",
      # Return options
      saveConsensusTOM = TRUE,
```

```
consensusTOMFilePattern = "consensusTOM-%a-Block%b.RData",
getCalibrationSamples = FALSE,

# Return the intermediate results as well?
keepIntermediateResults = saveConsensusTOM,

# Internal handling of TOMs
useDiskCache = NULL,
chunkSize = NULL,
cacheDir = ".",
cacheBase = ".blockConsModsCache",

# Behavior
collectGarbage = TRUE,
verbose = 1,
indent = 0)
```

Arguments

multiExpr Expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights optional observation weights in the same format (and dimensions) as multiExpr.

These weights are used for correlation calculations with data in multiExpr.

checkMissingData

Logical: should data be checked for excessive numbers of missing entries in

genes and samples, and for genes with zero variance? See details.

blocks Optional specification of blocks in which hierarchical clustering and module de-

tection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the correspond-

ing gene belongs.

maxBlockSize Integer giving maximum block size for module detection. Ignored if blocks

above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not

exceed maxBlockSize.

blockSizePenaltyPower

Number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block

size is very important.

nPreclusteringCenters

Number of centers to be used in the preclustering. Defaults to smaller of nGenes/20 and 100*nGenes/maxBlockSize, where nGenes is the number of genes (vari-

ables) in multiExpr.

randomSeed Integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit. If NULL is given,

the function will not save and restore the seed.

networkOptions A single list of class NetworkOptions giving options for network calculation for all of the networks, or a multiData structure containing one such list for each input data set.

keepIndividualTOMs

Logical: should individual TOMs be retained after the calculation is finished?

individualTOMFileNames

Character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

individualTOMInfo

A list, typically returned by individual TOMs, containing information about the topological overlap matrices in the individual data sets in multiExpr. See the output of individual TOMs for details on the content of the list.

consensusTree

A list specifying the consensus calculation. See details.

useBlocks

Optional vector giving the blocks that should be used for the calcualtions. If NULL, all all blocks will be used.

saveCalibratedIndividualTOMs

Logical: should the calibrated individual TOMs be saved?

calibratedIndividualTOMFilePattern

Specification of file names in which calibrated individual TOMs should be saved.

saveConsensusTOM

Logical: should the consensus TOM be saved to disk?

consensusTOMFilePattern

Character string giving the file names to save consensus TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error will be generated.

getCalibrationSamples

Logical: should the sampled values used for network calibration be returned?

keepIntermediateResults

Logical: should intermediate consensus TOMs be saved as well?

useDiskCache

Logical: should disk cache be used for consensus calculations? The disk cache can be used to store chunks of calibrated data that are small enough to fit one chunk from each set into memory (blocks may be small enough to fit one block of one set into memory, but not small enough to fit one block from all sets in a consensus calculation into memory at the same time). Using disk cache is slower but lessens the memory footprint of the calculation. As a general guide, if individual data are split into blocks, we recommend setting this argument to TRUE. If this argument is NULL, the function will decide whether to use disk cache based on the number of sets and block sizes.

chunkSize network similarities are saved in smaller chunks of size chunkSize. If NULL, an

appropriate chunk size will be determined from an estimate of available memory. Note that if the chunk size is greater than the memory required for storing

intemediate results, disk cache use will automatically be disabled.

cacheDir character string containing the directory into which cache files should be written.

The user should make sure that the filesystem has enough free space to hold the

cache files which can get quite large.

cacheBase character string containing the desired name for the cache files. The actual file

names will consists of cacheBase and a suffix to make the file names unique.

collectGarbage Logical: should garbage be collected after memory-intensive operations?

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function is essentially a wrapper for hierarchicalConsensusCalculation, with a few additional operations specific to calculations of topological overlaps.

Value

A list that contains the output of hierarchicalConsensusCalculation and two extra components:

individualTOMInfo

A copy of the input individual TOMInfo if it was non-NULL, or the result of

individualTOMs.

consensusTree A copy of the input consensusTree.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusCalculation for the actual hierarchical consensus calculation;

individual TOMs for the calculation of individual TOMs in a format suitable for consensus calculation.

 $hierarchical {\tt MergeCloseModules}$

Merge close (similar) hierarchical consensus modules

Description

Merges hierarchical consensus modules that are too close as measured by the correlation of their eigengenes.

Usage

```
hierarchicalMergeCloseModules(
  # input data
 multiExpr,
 multiExpr.imputed = NULL,
  labels,
  # Optional starting eigengenes
 MEs = NULL,
  unassdColor = if (is.numeric(labels)) 0 else "grey",
  # If missing data are present, impute them?
  impute = TRUE,
  # Options for eigengene network construction
  networkOptions,
  # Options for constructing the consensus
  consensusTree.
  calibrateMESimilarities = FALSE,
  # Merging options
  cutHeight = 0.2,
  iterate = TRUE,
  # Output options
  relabel = FALSE,
  colorSeq = NULL,
  getNewMEs = TRUE,
  getNewUnassdME = TRUE,
  # Options controlling behaviour of the function
  trapErrors = FALSE,
  verbose = 1, indent = 0)
```

Arguments

multiExpr Expression data in the multi-set format (see multiData). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiExpr.imputed

If multiExpr contain missing data, this argument can be used to supply the expression data with missing data imputed. If not given, the impute.knn function will be used to impute the missing data within each module (see imputeByModule.

labels A vector (numeric, character or a factor) giving module labels for genes (vari-

ables) in multiExpr.

MEs If module eigengenes have been calculated before, the user can save some com-

putational time by inputting them. MEs should have the same format as multiExpr.

If they are not given, they will be calculated.

unassdColor The label (value in labels) that represents unassigned genes. Module of this

label will not enter the module eigengene clustering and will not be merged

with other modules.

impute Should missing values be imputed in eigengene calculation? If imputation is dis-

abled, the presence of NA entries will cause the eigengene calculation to fail and eigengenes will be replaced by their hubgene approximation. See moduleEigengenes

for more details.

networkOptions A single list of class NetworkOptions giving options for network calculation

for all of the networks, or a multiData structure containing one such list for

each input data set.

consensusTree A list specifying the consensus calculation. See newConsensusTree for details.

calibrateMESimilarities

Logical: should module eigengene similarities be calibrated? This setting over-

rides the calibration options in consensusTree.

cutHeight Maximum dissimilarity (i.e., 1-correlation) that qualifies modules for merging.

iterate Controls whether the merging procedure should be repeated until there is no

change. If FALSE, only one iteration will be executed.

relabel Controls whether, after merging, color labels should be ordered by module size.

colorSeq Color labels to be used for relabeling. Defaults to the standard color order used

in this package if colors are not numeric, and to integers starting from 1 if

colors is numeric.

getNewMEs Controls whether module eigengenes of merged modules should be calculated

and returned.

getNewUnassdME When doing module eigengene manipulations, the function does not normally

calculate the eigengene of the 'module' of unassigned ('grey') genes. Setting this option to TRUE will force the calculation of the unassigned eigengene in the

returned newMEs, but not in the returned oldMEs.

trapErrors Controls whether computational errors in calculating module eigengenes, their

dissimilarity, and merging trees should be trapped. If TRUE, errors will be trapped and the function will return the input colors. If FALSE, errors will cause the func-

tion to stop.

verbose Controls verbosity of printed progress messages. 0 means silent, up to (about) 5

the verbosity gradually increases.

indent A single non-negative integer controlling indentation of printed messages. 0

means no indentation, each unit above that adds two spaces.

Details

This function merges input modules that are closely related. The similarities are quantified by correlations of module eigengenes; a "consensus" similarity is calculated using hierarchicalConsensusMEDissimilarity according to the recipe in consensusTree. Once the (dis-)similarities are calculated, average linkage hierarchical clustering of the module eigengenes is performed, the dendrogram is cut at the height cutHeight and modules on each branch are merged. The process is (optionally) repeated until no more modules are merged.

If, for a particular module, the module eigengene calculation fails, a hubgene approximation will be used.

The user should be aware that if a computational error occurs and trapErrors==TRUE, the returned list (see below) will not contain all of the components returned upon normal execution.

Value

If no errors occurred, a list with components

labels Labels for the genes corresponding to merged modules. The function attempts to

mimic the mode of the input labels: if the input labels is numeric, character and factor, respectively, so is the output. Note, however, that if the function performs relabeling, a standard sequence of labels will be used: integers starting at 1 if the input labels is numeric, and a sequence of color labels otherwise (see

colorSeg above).

dendro Hierarchical clustering dendrogram (average linkage) of the eigengenes of the

most recently computed tree. If iterate was set TRUE, this will be the dendrogram of the merged modules, otherwise it will be the dendrogram of the original

modules.

oldDendro Hierarchical clustering dendrogram (average linkage) of the eigengenes of the

original modules.

cutHeight The input cutHeight.

oldMEs Module eigengenes of the original modules in the sets given by useSets.

Module eigengenes of the merged modules in the sets given by useSets.

Module eigengenes of the merged modules in the sets given by useSets.

allOK A logical set to TRUE.

If an error occurred and trapErrors==TRUE, the list only contains these components:

colors A copy of the input colors. allOK a logical set to FALSE.

Author(s)

Peter Langfelder

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See Also

multiSetMEs for calculation of (consensus) module eigengenes across multiple data sets;

newConsensusTree for information about consensus trees;

hierarchicalConsensusMEDissimilarity for calculation of hierarchical consensus eigengene dissimilarity.

hubGeneSignificance

Hubgene significance

Description

Calculate approximate hub gene significance for all modules in network.

Usage

hubGeneSignificance(datKME, GS)

Arguments

datKME a data frame (or a matrix-like object) containing eigengene-based connectivities

of all genes in the network.

GS a vector with one entry for every gene containing its gene significance.

Details

In datKME rows correspond to genes and columns to modules.

Value

A vector whose entries are the hub gene significances for each module.

Author(s)

Steve Horvath

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

imputeByModule

 ${\tt ImmunePathwayLists}$

Immune Pathways with Corresponding Gene Markers

Description

This matrix gives a predefined set of marker genes for many immune response pathways, as assembled by Brian Modena (a member of Daniel R Salomon's lab at Scripps Research Institute), and colleagues. It is used with userListEnrichment to search user-defined gene lists for enrichment.

Usage

```
data(ImmunePathwayLists)
```

Format

A 3597 x 2 matrix of characters containing Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <Immune Pathway>__ImmunePathway. Note that the matrix is sorted first by Category and then by Gene, such that all genes related to the same category are listed sequentially.

Source

For more information about this list, please see userListEnrichment

Examples

```
data(ImmunePathwayLists)
head(ImmunePathwayLists)
```

imputeByModule

Impute missing data separately in each module

Description

Use impute.knn to ipmpute missing data, separately in each module.

Usage

```
imputeByModule(
  data,
  labels,
  excludeUnassigned = FALSE,
  unassignedLabel = if (is.numeric(labels)) 0 else "grey",
  scale = TRUE,
  ...)
```

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Arguments

data Data to be imputed, with variables (genes) in columns and observations (sam-

ples) in rows.

labels Module labels. A vector with one entry for each column in data.

excludeUnassigned

Logical: should unassigned variables (genes) be excluded from the imputation?

unassignedLabel

The value in labels that represents unassigned variables.

scale Logical: should data be scaled to mean 0 and variance 1 before imputation?

... Other arguments to impute.knn.

Value

The input data with missing values imputed.

Note

This function is potentially faster but could give different imputed values than applying impute.knn directly to (scaled) data.

Author(s)

Peter Langfelder

See Also

impute.knn that does the actual imputation.

individualTOMs

Calculate individual correlation network matrices

Description

This function calculates correlation network matrices (adjacencies or topological overlaps), after optionally first pre-clustering input data into blocks.

Usage

```
individualTOMs(
   multiExpr,
   multiWeights = NULL,
   multiExpr.imputed = NULL,

# Data checking options
   checkMissingData = TRUE,
```

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```
# Blocking options
blocks = NULL,
maxBlockSize = 5000,
blockSizePenaltyPower = 5,
nPreclusteringCenters = NULL,
randomSeed = 54321,

# Network construction options
networkOptions,

# Save individual TOMs?
saveTOMs = TRUE,
individualTOMFileNames = "individualTOM-Set%s-Block%b.RData",

# Behaviour options
collectGarbage = TRUE,
verbose = 2, indent = 0)
```

Arguments

multiExpr expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights

optional observation weights in the same format (and dimensions) as multiExpr. These weights are used for correlation calculations with data in multiExpr.

multiExpr.imputed

Optional version of multiExpr with missing data imputed. If not given and multiExpr contains missing data, they will be imputed using the function impute.knn.

checkMissingData

logical: should data be checked for excessive numbers of missing entries in genes and samples, and for genes with zero variance? See details.

blocks

optional specification of blocks in which hierarchical clustering and module detection should be performed. If given, must be a numeric vector with one entry per gene of multiExpr giving the number of the block to which the corresponding gene belongs.

maxBlockSize

integer giving maximum block size for module detection. Ignored if blocks above is non-NULL. Otherwise, if the number of genes in datExpr exceeds maxBlockSize, genes will be pre-clustered into blocks whose size should not exceed maxBlockSize.

blockSizePenaltyPower

number specifying how strongly blocks should be penalized for exceeding the maximum size. Set to a lrge number or Inf if not exceeding maximum block size is very important.

nPreclusteringCenters

number of centers to be used in the preclustering. Defaults to smaller of nGenes/20 and 100*nGenes/maxBlockSize, where nGenes is the number of genes (variables) in multiExpr.

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randomSeed integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit. If NULL is given,

the function will not save and restore the seed.

networkOptions A single list of class NetworkOptions giving options for network calculation

for all of the networks, or a multiData structure containing one such list for

each input data set.

saveTOMs logical: should individual TOMs be saved to disk (TRUE) or retuned directly in

the return value (FALSE)?

individualTOMFileNames

character string giving the file names to save individual TOMs into. The following tags should be used to make the file names unique for each set and block: %s will be replaced by the set number; %N will be replaced by the set name (taken from names(multiExpr)) if it exists, otherwise by set number; %b will be replaced by the block number. If the file names turn out to be non-unique, an error

will be generated.

collectGarbage Logical: should garbage collection be called after each block calculation? This

can be useful when the data are large, but could unnecessarily slow down calcu-

lation with small data.

verbose Integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent Indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The function starts by optionally filtering out samples that have too many missing entries and genes that have either too many missing entries or zero variance in at least one set. Genes that are filtered out are excluded from the network calculations.

If blocks is not given and the number of genes (columns) in multiExpr exceeds maxBlockSize, genes are pre-clustered into blocks using the function consensusProjectiveKMeans; otherwise all genes are treated in a single block. Any missing data in multiExpr will be imputed; if imputed data are already available, they can be supplied separately.

For each block of genes, the network adjacency is constructed and (if requested) topological overlap is calculated in each set. The topological overlaps can be saved to disk as RData files, or returned directly within the return value (see below). Note that the matrices can be big and returning them within the return value can quickly exhaust the system's memory. In particular, if the block-wise calculation is necessary, it is usually impossible to return all matrices in the return value.

Value

A list with the following components:

blockwiseAdjacencies

A multiData structure containing (possibly blockwise) network matrices for each input data set. The network matrices are stored as BlockwiseData objects.

setNames A copy of names(multiExpr).

nSets Number of sets in multiExpr

blockInfo A list of class BlockInformation, giving information about blocks and gene

and sample filtering.

networkOptions The input networkOptions, returned as a multiData structure with one entry

per input data set.

Author(s)

Peter Langfelder

See Also

Input arguments and output components of this function use multiData, NetworkOptions, BlockwiseData, and BlockInformation.

Underlying functions of interest include consensusProjectiveKMeans, TOMsimilarityFromExpr.

Inline display of progress

Inline display of progress

Description

These functions provide an inline display of pregress.

Usage

```
initProgInd(leadStr = "..", trailStr = "", quiet = !interactive())
updateProgInd(newFrac, progInd, quiet = !interactive())
```

Arguments

leadStr character string that will be printed before the actual progress number.

trailStr character string that will be printed after the actual progress number.

quiet can be used to silence the indicator for non-interactive sessions whose output is

typically redirected to a file.

newFrac new fraction of progress to be displayed.

progInd an object of class progressIndicator that encodes previously printed message.

Details

A progress indicator is a simple inline display of progress intended to satisfy impatient users during lengthy operations. The function initProgInd initializes a progress indicator (at zero); updateProgInd updates it to a specified fraction.

Note that excessive use of updateProgInd may lead to a performance penalty (see examples).

Value

Both functions return an object of class progressIndicator that holds information on the last printed value and should be used for subsequent updates of the indicator.

Author(s)

Peter Langfelder

Examples

```
max = 10;
prog = initProgInd("Counting: ", "done");
for (c in 1:max)
{
  Sys.sleep(0.10);
  prog = updateProgInd(c/max, prog);
}
printFlush("");
printFlush("Example 2:");
prog = initProgInd();
for (c in 1:max)
  Sys.sleep(0.10);
  prog = updateProgInd(c/max, prog);
}
printFlush("");
## Example of a significant slowdown:
## Without progress indicator:
system.time( \{a = 0; for (i in 1:10000) a = a+i; \})
## With progress indicator, some 50 times slower:
system.time(
  {
   prog = initProgInd("Counting: ", "done");
   a = 0;
   for (i in 1:10000)
    {
      a = a+i;
      prog = updateProgInd(i/10000, prog);
  }
)
```

intramodular Connectivity

Calculation of intramodular connectivity

Description

Calculates intramodular connectivity, i.e., connectivity of nodes to other nodes within the same module.

Usage

Arguments

adjMat	adjacency matrix, a square, symmetric matrix with entries between 0 and 1.
colors	module labels. A vector of length ncol(adjMat) giving a module label for each gene (node) of the network.
scaleByMax	logical: should intramodular connectivities be scaled by the maximum IM connectivity in each module?
datExpr	data frame or matrix containing expression data. Columns correspond to genes and rows to samples.
corFnc	character string specifying the function to be used to calculate co-expression similarity for correlation networks. Defaults to Pearson correlation. Any function returning values between -1 and 1 can be used.
corOptions	character string specifying additional arguments to be passed to the function given by corFnc. Use "use = 'p', method = 'spearman'" to obtain Spearman correlation.
weights	optional matrix of the same dimensions as datExpr, giving the weights for individual observations in datExpr. These will be passed on to the correlation function.
distFnc	character string specifying the function to be used to calculate co-expression similarity for distance networks. Defaults to the function dist. Any function returning non-negative values can be used.

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distOptions character string specifying additional arguments to be passed to the function

given by distFnc. For example, when the function dist is used, the argument

method can be used to specify various ways of computing the distance.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid", "distance".

power soft thresholding power.

ignoreColors level(s) of colors that identifies unassigned genes. The intramodular connec-

tivity in this "module" will not be calculated.

getWholeNetworkConnectivity

logical: should whole-network connectivity be computed as well? For large

networks, this can be quite time-consuming.

Details

The module labels can be numeric or character. For each node (gene), the function sums adjacency entries (excluding the diagonal) to other nodes within the same module. Optionally, the connectivities can be scaled by the maximum connectivy in each module.

Value

If input getWholeNetworkConnectivity is TRUE, a data frame with 4 columns giving the total connectivity, intramodular connectivity, extra-modular connectivity, and the difference of the intraand extra-modular connectivities for all genes; otherwise a vector of intramodular connectivities,

Author(s)

Steve Horvath and Peter Langfelder

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

See Also

adjacency

isMultiData

Determine whether the supplied object is a valid multiData structure

Description

Attempts to determine whether the supplied object is a valid multiData structure (see Details).

Usage

```
isMultiData(x, strict = TRUE)
```

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Arguments

x An object.

strict Logical: should the structure of multiData be checked for "strict" compliance?

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

This function checks whether the supplied x is a multiData structure in the "strict" (when strict = TRUE or "loose" strict = FALSE sense.

Value

Logical: TRUE if the input x is a multiData structure, FALSE otherwise.

Author(s)

Peter Langfelder

See Also

Other multiData handling functions whose names start with mtd.

keepCommonProbes

Keep probes that are shared among given data sets

Description

This function strips out probes that are not shared by all given data sets, and orders the remaining common probes using the same order in all sets.

Usage

```
keepCommonProbes(multiExpr, orderBy = 1)
```

Arguments

multiExpr expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

orderBy index of the set by which probes are to be ordered.

Value

Expression data in the same format as the input data, containing only common probes.

Author(s)

Peter Langfelder

See Also

checkSets

kMEcomparisonScatterplot

Function to plot kME values between two comparable data sets.

Description

Plots the kME values of genes in two groups of expression data for each module in an inputted color vector.

Usage

Arguments

datExpr1	The first expression matrix (samples=rows, genes=columns). This can either include only the data for group A (in which case dataExpr2 must be entered), or can contain all of the data for groups A and B (in which case in A and in B must be entered).
datExpr2	The second expression matrix, or set to NULL if all data is from same expression matrix. If entered, datExpr2 must contain the same genes as datExpr1 in the same order.
colorh	The common color vector (module labels) corresponding to both sets of expression data.

inA, inB	Vectors of TRUE/FALSE indicating whether a sample is in group A/B, or a vector of numeric indices indicating which samples are in group A/B. If datExpr2 is entered, these inputs are ignored (thus default = NULL). For these and all other A/B inputs, "A" corresponds to datExpr1 and "B" corresponds to datExpr2 if datExpr2 is entered; otherwise "A" corresponds to datExpr1[inA,] while "B" corresponds to datExpr1[inB,].
MEsA, MEsB	Either the module eigengenes or NULL (default) in which case the module eigengenes will be calculated. In inputted, MEs MUST be calculated using "moduleEigengenes(<pre>parameters>)\$eigengenes" for function to work properly.</pre>
nameA, nameB	The names of these groups (defaults = "A" and "B"). The resulting file name (see below) and x and y axis labels for each scatter plot depend on these names.
plotAll	If TRUE, plot gene-ME correlations for all genes. If FALSE, plot correlations for only genes in the plotted module (default). Note that the output file name will be different depending on this parameter, so both can be run without overwriting results.
noGrey	If TRUE (default), the grey module genes are ignored. This parameter is only used if MEsA and MEsB are calculated.
maxPlot	The maximum number of random genes to include (default=1000). Smaller values lead to smaller and less cluttered plots, usually without significantly affecting the resulting correlations. This parameter is only used if plotAll=TRUE.
pch	See help file for "points". Setting pch=19 (default) produces solid circles.
fileName	Name of the file to hold the plots. Since the output format is pdf, the extension should be .pdf .
	Other plotting parameters that are allowable inputs to verboseScatterplot.

Value

The default output is a file called "kME_correlations_between_[nameA]_and_[nameB]_[all/inMod].pdf", where [nameA] and [nameB] correspond to the nameA and nameB input parameters, and [all/inMod] depends on whether plotAll=TRUE or FALSE. This output file contains all of the plots as separate pdf images, and will be located in the current working directory.

Note

The function "pdf", which can be found in the grDevices library, is required to run this function.

Author(s)

Jeremy Miller

Examples

```
# Example output file ("kME_correlations_between_A_and_B_inMod.pdf") using simulated data.
## Not run:
set.seed = 100
ME=matrix(0,50,5)
for (i in 1:5) ME[,i]=sample(1:100,50)
```

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 ${\tt labeledBarplot}$

Barplot with text or color labels.

Description

Produce a barplot with extra annotation.

Usage

```
labeledBarplot(
    Matrix, labels,
    colorLabels = FALSE,
    colored = TRUE,
    setStdMargins = TRUE,
    stdErrors = NULL,
    cex.lab = NULL,
    xLabelsAngle = 45,
    ...)
```

Arguments

Matrix	vector or a matrix to be plotted.
labels	labels to annotate the bars underneath the barplot.
colorLabels	logical: should the labels be interpreted as colors? If TRUE, the bars will be labeled by colored squares instead of text. See details.
colored	logical: should the bars be divided into segments and colored? If TRUE, assumes the labels can be interpreted as colors, and the input Matrix is square and the rows have the same labels as the columns. See details.
setStdMargins	if TRUE, the function wil set margins c(3, 3, 2, 2)+0.2.
stdErrors	if given, error bars corresponding to 1.96*stdErrors will be plotted on top of the bars.
cex.lab	character expansion factor for axis labels, including the text labels underneath the barplot.
xLabelsAngle	angle at which text labels under the barplot will be printed.
	other parameters for the function barplot.

Details

Individual bars in the barplot can be identified either by printing the text of the corresponding entry in labels underneath the bar at the angle specified by xLabelsAngle, or by interpreting the labels entry as a color (see below) and drawing a correspondingly colored square underneath the bar.

For reasons of compatibility with other functions, labels are interpreted as colors after stripping the first two characters from each label. For example, the label "MEturquoise" is interpreted as the color turquoise.

If colored is set, the code assumes that labels can be interpreted as colors, and the input Matrix is square and the rows have the same labels as the columns. Each bar in the barplot is then sectioned into contributions from each row entry in Matrix and is colored by the color given by the entry in labels that corresponds to the row.

Value

None.

Author(s)

Peter Langfelder

labeledHeatmap

Produce a labeled heatmap plot

Description

Plots a heatmap plot with color legend, row and column annotation, and optional text within th heatmap.

Usage

```
labeledHeatmap(
 Matrix.
  xLabels, yLabels = NULL,
  xSymbols = NULL, ySymbols = NULL,
  colorLabels = NULL,
  xColorLabels = FALSE, yColorLabels = FALSE,
  checkColorsValid = TRUE,
  invertColors = FALSE,
  setStdMargins = TRUE,
  xLabelsPosition = "bottom",
  xLabelsAngle = 45,
  xLabelsAdj = 1,
  yLabelsPosition = "left",
  xColorWidth = 2 * strheight("M"),
  yColorWidth = 2 * strwidth("M"),
  xColorOffset = strheight("M")/3,
```

```
yColorOffset = strwidth("M")/3,
colorMatrix = NULL,
colors = NULL,
naColor = "grey"
textMatrix = NULL,
cex.text = NULL,
textAdj = c(0.5, 0.5),
cex.lab = NULL,
cex.lab.x = cex.lab,
cex.lab.y = cex.lab,
colors.lab.x = 1,
colors.lab.y = 1,
font.lab.x = 1,
font.lab.y = 1,
bg.lab.x = NULL,
bg.lab.y = NULL,
x.adj.lab.y = 1,
plotLegend = TRUE,
keepLegendSpace = plotLegend,
legendLabel = "",
cex.legendLabel = 1,
# Separator line specification
verticalSeparator.x = NULL,
verticalSeparator.col = 1,
verticalSeparator.lty = 1,
verticalSeparator.lwd = 1,
verticalSeparator.ext = 0,
verticalSeparator.interval = 0,
horizontalSeparator.y = NULL,
horizontalSeparator.col = 1,
horizontalSeparator.lty = 1,
horizontalSeparator.lwd = 1,
horizontalSeparator.ext = 0,
horizontalSeparator.interval = 0,
# optional restrictions on which rows and columns to actually show
showRows = NULL,
showCols = NULL,
...)
```

Arguments

```
Matrix numerical matrix to be plotted in the heatmap.

xLabels labels for the columns. See Details.

yLabels labels for the rows. See Details.
```

xSymbols additional labels used when xLabels are interpreted as colors. See Details. ySymbols additional labels used when yLabels are interpreted as colors. See Details. colorLabels logical: should xLabels and yLabels be interpreted as colors? If given, overrides xColorLabels and yColorLabels below. xColorLabels logical: should xLabels be interpreted as colors? yColorLabels logical: should yLabels be interpreted as colors? checkColorsValid logical: should given colors be checked for validity against the output of colors() ? If this argument is FALSE, invalid color specification will trigger an error. invertColors logical: should the color order be inverted? setStdMargins logical: should standard margins be set before calling the plot function? Standard margins depend on colorLabels: they are wider for text labels and narrower for color labels. The defaults are static, that is the function does not attempt to guess the optimal margins. xLabelsPosition a character string specifying the position of labels for the columns. Recognized values are (unique abbreviations of) "top", "bottom". xLabelsAngle angle by which the column labels should be rotated. xLabelsAdj justification parameter for column labels. See par and the description of parameter "adj". yLabelsPosition a character string specifying the position of labels for the columns. Recognized values are (unique abbreviations of) "left", "right". xColorWidth width of the color labels for the x axis expressed in user corrdinates. yColorWidth width of the color labels for the y axis expressed in user coordinates. xColorOffset gap between the y axis and color labels, in user coordinates. yColorOffset gap between the x axis and color labels, in user coordinates. colorMatrix optional explicit specification for the color of the heatmap cells. If given, overrides values specified in colors and naColor. colors color pallette to be used in the heatmap. Defaults to heat.colors. Only used if colorMatrix is not given. naColor color to be used for encoding missing data. Only used if colorMatrix is not used. optional text entries for each cell. Either a matrix of the same dimensions as textMatrix Matrix or a vector of the same length as the number of entries in Matrix. cex.text character expansion factor for textMatrix. textAdj Adjustment for the entries in the text matrix. See the adj argument to text. cex.lab character expansion factor for text labels labeling the axes. cex.lab.x character expansion factor for text labels labeling the x axis. Overrides cex.lab

character expansion factor for text labels labeling the y axis. Overrides cex.lab

cex.lab.y

above.

colors.lab.x	colors for character labels or symbols along x axis.
colors.lab.y	colors for character labels or symbols along y axis.
font.lab.x	integer specifying font for labels or symbols along x axis. See text.
font.lab.y	integer specifying font for labels or symbols along y axis. See text.
bg.lab.x	background color for the margin along the x axis.
bg.lab.y	background color for the margin along the y axs.
x.adj.lab.y	Justification of labels for the y axis along the x direction. A value of 0 produces left-justified text, 0.5 (the default) centered text and 1 right-justified text.
plotLegend	logical: should a color legend be plotted?

keepLegendSpace

logical: if the color legend is not drawn, should the space be left empty (TRUE), or should the heatmap fill the space (FALSE)?

legendLabel character string to be shown next to the label analogous to an axis label.

cex.legendLabel

character expansion factor for the legend label.

verticalSeparator.x

indices of columns in input Matrix after which separator lines (vertical lines between columns) should be drawn. NULL means no lines will be drawn.

verticalSeparator.col

color(s) of the vertical separator lines. Recycled if need be.

verticalSeparator.lty

line type of the vertical separator lines. Recycled if need be.

verticalSeparator.lwd

line width of the vertical separator lines. Recycled if need be.

verticalSeparator.ext

number giving the extension of the separator line into the margin as a fraction of the margin width. 0 means no extension, 1 means extend all the way through the margin.

verticalSeparator.interval

number giving the interval for vertical separators. If larger than zero, vertical separators will be drawn after every vertical Separator. interval of displayed columns. Used only when length of verticalSeparator.x is zero.

horizontalSeparator.y

indices of columns in input Matrix after which separator lines (horizontal lines between columns) should be drawn. NULL means no lines will be drawn.

horizontalSeparator.col

color(s) of the horizontal separator lines. Recycled if need be.

horizontalSeparator.lty

line type of the horizontal separator lines. Recycled if need be.

horizontalSeparator.lwd

line width of the horizontal separator lines. Recycled if need be.

horizontalSeparator.ext

number giving the extension of the separator line into the margin as a fraction of the margin width. 0 means no extension, 1 means extend all the way through the margin.

horizontalSeparator.interval

number giving the interval for horizontal separators. If larger than zero, horizontal separators will be drawn after every horizontalSeparator.interval of displayed rows. Used only when length of horizontalSeparator.y is zero.

showRows A numeric vector giving the indices of rows that are actually to be shown. De-

faults to all rows.

showCols A numeric vector giving the indices of columns that are actually to be shown.

Defaults to all columns.

... other arguments to function heatmap.

Details

The function basically plots a standard heatmap plot of the given Matrix and embellishes it with row and column labels and/or with text within the heatmap entries. Row and column labels can be either character strings or color squares, or both.

To get simple text labels, use colorLabels=FALSE and pass the desired row and column labels in yLabels and xLabels, respectively.

To label rows and columns by color squares, use colorLabels=TRUE; yLabels and xLabels are then expected to represent valid colors. For reasons of compatibility with other functions, each entry in yLabels and xLabels is expected to consist of a color designation preceded by 2 characters: an example would be MEturquoise. The first two characters can be arbitrary, they are stripped. Any labels that do not represent valid colors will be considered text labels and printed in full, allowing the user to mix text and color labels.

It is also possible to label rows and columns by both color squares and additional text annotation. To achieve this, use the above technique to get color labels and, additionally, pass the desired text annotation in the xSymbols and ySymbols arguments.

Value

None.

Author(s)

Peter Langfelder

See Also

heatmap, colors

Examples

```
# This example illustrates 4 main ways of annotating columns and rows of a heatmap.
```

- # Copy and paste the whole example into an R session with an interactive plot window;
- # alternatively, you may replace the command sizeGrWindow below by opening
- # another graphical device such as pdf.

```
# Generate a matrix to be plotted
```

```
nCol = 8; nRow = 7;
```

```
mat = matrix(runif(nCol*nRow, min = -1, max = 1), nRow, nCol);
rowColors = standardColors(nRow);
colColors = standardColors(nRow + nCol)[(nRow+1):(nRow + nCol)];
rowColors;
colColors;
sizeGrWindow(9,7)
par(mfrow = c(2,2))
par(mar = c(4, 5, 4, 6));
# Label rows and columns by text:
labeledHeatmap(mat, xLabels = colColors, yLabels = rowColors,
               colors = greenWhiteRed(50),
               setStdMargins = FALSE,
               textMatrix = signif(mat, 2),
               main = "Text-labeled heatmap");
# Label rows and columns by colors:
rowLabels = paste("ME", rowColors, sep="");
colLabels = paste("ME", colColors, sep="");
labeledHeatmap(mat, xLabels = colLabels, yLabels = rowLabels,
               colorLabels = TRUE,
               colors = greenWhiteRed(50),
               setStdMargins = FALSE,
               textMatrix = signif(mat, 2),
               main = "Color-labeled heatmap");
# Mix text and color labels:
rowLabels[3] = "Row 3";
colLabels[1] = "Column 1";
labeledHeatmap(mat, xLabels = colLabels, yLabels = rowLabels,
               colorLabels = TRUE,
               colors = greenWhiteRed(50),
               setStdMargins = FALSE,
               textMatrix = signif(mat, 2),
               main = "Mix-labeled heatmap");
# Color labels and additional text labels
rowLabels = paste("ME", rowColors, sep="");
colLabels = paste("ME", colColors, sep="");
extraRowLabels = paste("Row", c(1:nRow));
extraColLabels = paste("Column", c(1:nCol));
# Extend margins to fit all labels
```

labeledHeatmap.multiPage

Labeled heatmap divided into several separate plots.

Description

This function produces labaled heatmaps divided into several plots. This is useful for large heatmaps where labels on individual columns and rows may become unreadably small (or overlap).

Usage

```
labeledHeatmap.multiPage(
    # Input data and ornaments
    Matrix,
    xLabels, yLabels = NULL,
    xSymbols = NULL, ySymbols = NULL,
    textMatrix = NULL,

# Paging options
    rowsPerPage = NULL, maxRowsPerPage = 20,
    colsPerPage = NULL, maxColsPerPage = 10,
    addPageNumberToMain = TRUE,

# Further arguments to labeledHeatmap
    zlim = NULL,
    signed = TRUE,
    main = "",
    ...)
```

Arguments

Matrix	numerical matrix to be plotted in the heatmap.
xLabels	labels for the columns. See Details.
yLabels	labels for the rows. See Details.
xSymbols	additional labels used when xLabels are interpreted as colors. See Details.
ySymbols	additional labels used when yLabels are interpreted as colors. See Details.

optional text entries for each cell. Either a matrix of the same dimensions as Matrix or a vector of the same length as the number of entries in Matrix.

rowsPerPage optional list in which each component is a vector specifying which rows should

appear together in each plot. If not given, will be generated automatically based

on maxRowsPerPage below and the number of rows in Matrix.

maxRowsPerPage integer giving maximum number of rows appearing on each plot (page).

colsPerPage optional list in which each component is a vector specifying which columns

should appear together in each plot. If not given, will be generated automatically

based on ${\tt maxColsPerPage}$ below and the number of rows in ${\tt Matrix}$.

maxColsPerPage integer giving maximum number of columns appearing on each plot (page). addPageNumberToMain

logical: should plot/page number be added to the main title of each plot?

zlim Optional specification of the extreme values for the color scale. If not given,

will be determined from the input Matrix.

signed logical: should the input Matrix be converted to colors using a scale centered at

zero?

main Main title for each plot/page, optionally with the plot/page number added.

... other arguments to function labeledHeatmap.

Details

The function labeledHeatmap is used to produce each plot/page; most arguments are described in more detail in the help file for that function.

In each plot/page labeledHeatmap plots a standard heatmap plot of an appropriate sub-rectangle of Matrix and embellishes it with row and column labels and/or with text within the heatmap entries. Row and column labels can be either character strings or color squares, or both.

To get simple text labels, use colorLabels=FALSE and pass the desired row and column labels in yLabels and xLabels, respectively.

To label rows and columns by color squares, use colorLabels=TRUE; yLabels and xLabels are then expected to represent valid colors. For reasons of compatibility with other functions, each entry in yLabels and xLabels is expected to consist of a color designation preceded by 2 characters: an example would be MEturquoise. The first two characters can be arbitrary, they are stripped. Any labels that do not represent valid colors will be considered text labels and printed in full, allowing the user to mix text and color labels.

It is also possible to label rows and columns by both color squares and additional text annotation. To achieve this, use the above technique to get color labels and, additionally, pass the desired text annotation in the xSymbols and ySymbols arguments.

If rowsPerPage (colsPerPage) is not given, rows (columns) are allocated automatically as uniformly as possible, in contiguous blocks of size at most maxRowsPerPage (maxColsPerPage). The allocation is performed by the function allocateJobs.

Value

None.

210 labelPoints

Author(s)

Peter Langfelder

See Also

The workhorse function labeledHeatmap for the actual heatmap plot; function allocateJobs for the allocation of rows/columns to each plot.

labelPoints

Label scatterplot points

Description

Given scatterplot point coordinates, the function tries to place labels near the points such that the labels overlap as little as possible. User beware: the algorithm implemented here is quite primitive and while it will help in many cases, it is by no means perfect. Consider this function experimental. We hope to improve the algorithm in the future to make it useful in a broader range of situations.

Usage

```
labelPoints(
   x, y, labels,
   cex = 0.7, offs = 0.01, xpd = TRUE,
   jiggle = 0, protectEdges = TRUE,
   doPlot = TRUE, ...)
```

Arguments

X	a vector of x coordinates of the points
у	a vector of y coordinates of the points
labels	labels to be placed next to the points
cex	character expansion factor for the labels
offs	offset of the labels from the plotted coordinates in inches
xpd	logical: controls truncating labels to fit within the plotting region. See par.
jiggle	amount of random noise to be added to the coordinates. This may be useful if the scatterplot is too regular (such as all points on one straight line).
protectEdges	logical: should labels be shifted inside the (actual or virtual) frame of the plot?
doPlot	logical: should the labels be actually added to the plot? Value FALSE may be useful if the user would like to simply compute the best label positions the function can come up with.
	other arguments to function text.

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Details

The algorithm basically works by finding the direction of most surrounding points, and attempting to place the label in the opposite direction. There are (not uncommon) situations in which this placement is suboptimal; the author promises to further develop the function sometime in the future.

Note that this function does not plot the actual scatterplot; only the labels are plotted. Plotting the scatterplot is the responsibility of the user.

The argument offs needs to be carefully tuned to the size of the plotted symbols. Sorry, no automation here yet.

The argument protectEdges can be used to shift labels that would otherwise extend beyond the plot to within the plot. Sometimes this may cause some overlapping with other points or labels; use with care.

Value

Invisibly, a data frame with 3 columns, giving the x and y positions of the labels, and the labels themselves.

Author(s)

Peter Langfelder

See Also

```
plot.default, text
```

Examples

212 labels2colors

labels2colors Convert numerical labels to colors.

Description

Converts a vector or array of numerical labels into a corresponding vector or array of colors corresponding to the labels.

Usage

Arguments

labels	Vector or matrix of non-negative integer or other (such as character) labels. See details.
zeroIsGrey	If TRUE, labels 0 will be assigned color grey. Otherwise, labels below 1 will trigger an error.
colorSeq	Color sequence corresponding to labels. If not given, a standard sequence will be used.
naColor	Color that will encode missing values.

logical: if labels is a matrix, should each column have its own colors?

Details

If labels is numeric, it is used directly as index to the standard color sequence. If 0 is present among the labels and zeroIsGrey=TRUE, labels 0 are given grey color.

If labels is not numeric, its columns are turned into factors and the numeric representation of each factor is used to assign the corresponding colors. In this case commonColorCode governs whether each column gets its own color code, or whether the color code will be universal.

The standard sequence start with well-distinguishable colors, and after about 40 turns into a quasirandom sampling of all colors available in R with the exception of all shades of grey (and gray).

If the input labels have a dimension attribute, it is copied into the output, meaning the dimensions of the returned value are the same as those of the input labels.

Value

A vector or array of character strings of the same length or dimensions as labels.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

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Examples

```
labels = c(0:20);
labels2colors(labels);
labels = matrix(letters[1:9], 3,3);
labels2colors(labels)
# Note the difference when commonColorCode = FALSE
labels2colors(labels, commonColorCode = FALSE)
```

list2multiData

Convert a list to a multiData structure and vice-versa.

Description

list2multiData converts a list to a multiData structure; multiData2list does the inverse.

Usage

```
list2multiData(data)
multiData2list(multiData)
```

Arguments

data A list to be converted to a multiData structure.

multiData A multiData structure to be converted to a list.

Details

A multiData structure is a vector of lists (one list for each set) where each list has a component data containing some useful information.

Value

For list2multiData, a multiData structure; for multiData2list, the corresponding list.

Author(s)

Peter Langfelder

214 lowerTri2matrix

lowerTri2matrix	Reconstruct a symmetric matrix from a distance (lower-triangular)
	representation

Description

Assuming the input vector contains a vectorized form of the distance representation of a symmetric matrix, this function creates the corresponding matrix. This is useful when re-forming symmetric matrices that have been vectorized to save storage space.

Usage

```
lowerTri2matrix(x, diag = 1)
```

Arguments

```
x a numeric vector
diag value to be put on the diagonal. Recycled if necessary.
```

Details

The function assumes that x contains the vectorized form of the distance representation of a symmetric matrix. In particular, x must have a length that can be expressed as n*(n-1)/2, with n an integer. The result of the function is then an n times n matrix.

Value

A symmetric matrix whose lower triangle is given by x.

Author(s)

Peter Langfelder

Examples

```
# Create a symmetric matrix
m = matrix(c(1:16), 4,4)
mat = (m + t(m));
diag(mat) = 0;

# Print the matrix
mat

# Take the lower triangle and vectorize it (in two ways)
x1 = mat[lower.tri(mat)]
x2 = as.vector(as.dist(mat))

all.equal(x1, x2) # The vectors are equal
```

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```
# Turn the vectors back into matrices
new.mat = lowerTri2matrix(x1, diag = 0);
# Did we get back the same matrix?
all.equal(mat, new.mat)
```

 ${\tt matchLabels}$

Relabel module labels to best match the given reference labels

Description

Given a source and reference vectors of module labels, the function produces a module labeling that is equivalent to source, but individual modules are re-labeled so that modules with significant overlap in source and reference have the same labels.

Usage

Arguments

source	a vector or a matrix of reference labels. The labels may be numeric or character.
reference	a vector of reference labels.
pThreshold	threshold of Fisher's exact test for considering modules to have a significant overlap.
na.rm	logical: should missing values in either source or reference be removed? If not, missing values may be treated as a standard label or the function may throw an error (exact behaviour depends on whether the input labels are numeric or not).
ignoreLabels	labels in source and reference to be considered unmatchable. These labels are excluded from the re-labeling procedure.
extraLabels	a vector of labels for modules in source that cannot be matched to any modules in reference. The user should ensure that this vector contains enough labels since the function automatically removes a values that occur in either source,

reference or ignoreLabels, to avoid possible confusion.

216 matrixToNetwork

Details

Each column of source is treated separately. Unlike in previous version of this function, source and reference labels can be any labels, not necessarily of the same type.

The function calculates the overlap of the source and reference modules using Fisher's exact test. It then attempts to relabel source modules such that each source module gets the label of the reference module that it overlaps most with, subject to not renaming two source modules to the same reference module. (If two source modules point to the same reference module, the one with the more significant overlap is chosen.)

Those source modules that cannot be matched to a reference module are labeled using those labels from extraLabels that do not occur in either of source, reference or ignoreLabels.

Value

A vector (if the input source labels are a vector) or a matrix (if the input source labels are a matrix) of the new labels.

Author(s)

Peter Langfelder

See Also

overlapTable for calculation of overlap counts and p-values; standardColors for standard non-numeric WGCNA labels.

matrixToNetwork

Construct a network from a matrix

Description

Constructs a network

Usage

```
matrixToNetwork(
   mat,
   symmetrizeMethod = c("average", "min", "max"),
   signed = TRUE,
   min = NULL, max = NULL,
   power = 12,
   diagEntry = 1)
```

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Arguments

matrix to be turned into a network. Must be square.

symmetrizeMethod

method for symmetrizing the matrix. The method will be applied to each com-

ponent of mat and its transpose.

signed logical: should the resulting network be signed? Unsigned networks are con-

structed from abs(mat).

min minimum allowed value for mat. If NULL, the actual attained minimum of mat

will be used. Missing data are ignored. Values below min are truncated to min.

max maximum allowed value for mat. If NULL, the actual attained maximum of mat

will be used. Missing data are ignored. Values below max are truncated to max.

power the soft-thresholding power.

diagEntry the value of the entries on the diagonal in the result. This is usally 1 but some

applications may require a zero (or even NA) diagonal.

Details

If signed is FALSE, the matrix mat is first converted to its absolute value.

This function then symmetrizes the matrix using the symmetrizeMethod component-wise on mat and t(mat) (i.e., the transpose of mat).

In the next step, the symmetrized matrix is linearly scaled to the interval [0,1] using either min and max (each either supplied or determined from the matrix). Values outside of the [min, max] range are truncated to min or max.

Lastly, the adjacency is calculated by rasing the matrix to power. The diagonal of the result is set to diagEntry. Note that most WGCNA functions expect the diagonal of an adjacency matrix to be 1.

Value

The adjacency matrix that encodes the network.

Author(s)

Peter Langfelder

See Also

adjacency for calculation of a correlation network (adjacency) from a numeric matrix such as expression data

adjacency.fromSimilarity for simpler calculation of a network from a symmetric similarity matrix.

218 mergeCloseModules

mergeCloseModules

Merge close modules in gene expression data

Description

Merges modules in gene expression networks that are too close as measured by the correlation of their eigengenes.

Usage

```
mergeCloseModules(
# input data
 exprData, colors,
  # Optional starting eigengenes
 MEs = NULL,
  # Optional restriction to a subset of all sets
  useSets = NULL,
  # If missing data are present, impute them?
  impute = TRUE,
  # Input handling options
  checkDataFormat = TRUE,
  unassdColor = if (is.numeric(colors)) 0 else "grey",
  # Options for eigengene network construction
  corFnc = cor, corOptions = list(use = 'p'),
  useAbs = FALSE,
  # Options for constructing the consensus
  equalizeQuantiles = FALSE,
  quantileSummary = "mean",
  consensusQuantile = 0,
  # Merging options
  cutHeight = 0.2,
  iterate = TRUE,
  # Output options
  relabel = FALSE,
  colorSeq = NULL,
  getNewMEs = TRUE,
 getNewUnassdME = TRUE,
  # Options controlling behaviour of the function
```

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```
trapErrors = FALSE,
verbose = 1, indent = 0)
```

Arguments

exprData Expression data, either a single data frame with rows corresponding to sam-

ples and columns to genes, or in a multi-set format (see checkSets). See

checkDataStructure below.

colors A vector (numeric, character or a factor) giving module colors for genes. The

method only makes sense when genes have the same color label in all sets, hence

a single vector.

MEs If module eigengenes have been calculated before, the user can save some com-

putational time by inputting them. MEs should have the same format as exprData.

If they are not given, they will be calculated.

useSets A vector of scalar allowing the user to specify which sets will be used to cal-

culate the consensus dissimilarity of module eigengenes. Defaults to all given

sets.

impute Should missing values be imputed in eigengene calculation? If imputation is dis-

abled, the presence of NA entries will cause the eigengene calculation to fail and eigengenes will be replaced by their hubgene approximation. See moduleEigengenes

for more details.

checkDataFormat

If TRUE, the function will check exprData and MEs for correct multi-set structure. If single set data is given, it will be converted into a format usable for the

function. If FALSE, incorrect structure of input data will trigger an error.

unassdColor Specifies the string that labels unassigned genes. Module of this color will not

enter the module eigengene clustering and will not be merged with other mod-

ules.

corFnc Correlation function to be used to calculate correlation of module eigengenes.

corOptions Can be used to specify options to the correlation function, in addition to argu-

ment x which is used to pass the actual data to calculate the correlation of.

useAbs Specifies whether absolute value of correlation or plain correlation (of module

eigengenes) should be used in calculating module dissimilarity.

equalizeQuantiles

Logical: should quantiles of the eigengene dissimilarity matrix be equalized ("quantile normalized")? The default is FALSE for reproducibility of old code; when there are many eigengenes (e.g., at least 50), better results may be achieved

if quantile equalization is used.

quantileSummary

One of "mean" or "median". Controls how a reference dissimilarity is computed from the input ones (using mean or median, respectively).

consensusQuantile

A number giving the desired quantile to use in the consensus similarity calculation (see details).

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cutHeight Maximum dissimilarity (i.e., 1-correlation) that qualifies modules for merging. Controls whether the merging procedure should be repeated until there is no iterate change. If FALSE, only one iteration will be executed. relabel Controls whether, after merging, color labels should be ordered by module size. colorSeq Color labels to be used for relabeling. Defaults to the standard color order used in this package if colors are not numeric, and to integers starting from 1 if colors is numeric. getNewMEs Controls whether module eigengenes of merged modules should be calculated and returned. When doing module eigengene manipulations, the function does not normally getNewUnassdME calculate the eigengene of the 'module' of unassigned ('grey') genes. Setting this option to TRUE will force the calculation of the unassigned eigengene in the returned newMEs, but not in the returned oldMEs. trapErrors Controls whether computational errors in calculating module eigengenes, their dissimilarity, and merging trees should be trapped. If TRUE, errors will be trapped and the function will return the input colors. If FALSE, errors will cause the function to stop. Controls verbosity of printed progress messages. 0 means silent, up to (about) 5 verbose the verbosity gradually increases. indent A single non-negative integer controlling indentation of printed messages. 0

Details

This function merges input modules that are closely related. The similarities are measured by correlations of module eigengenes; a "consensus" measure is defined as the "consensus quantile" over the corresponding relationship in each set. Once the (dis-)similarity is calculated, average linkage hierarchical clustering of the module eigengenes is performed, the dendrogram is cut at the height cutHeight and modules on each branch are merged. The process is (optionally) repeated until no more modules are merged.

means no indentation, each unit above that adds two spaces.

If, for a particular module, the module eigengene calculation fails, a hubgene approximation will be used.

The user should be aware that if a computational error occurs and trapErrors==TRUE, the returned list (see below) will not contain all of the components returned upon normal execution.

Value

If no errors occurred, a list with components

colors

Color labels for the genes corresponding to merged modules. The function attempts to mimic the mode of the input colors: if the input colors is numeric, character and factor, respectively, so is the output. Note, however, that if the function performs relabeling, a standard sequence of labels will be used: integers starting at 1 if the input colors is numeric, and a sequence of color labels otherwise (see colorSeq above).

dendro Hierarchical clustering dendrogram (average linkage) of the eigengenes of the

most recently computed tree. If iterate was set TRUE, this will be the dendrogram of the merged modules, otherwise it will be the dendrogram of the original

modules.

oldDendro Hierarchical clustering dendrogram (average linkage) of the eigengenes of the

original modules.

cutHeight The input cutHeight.

oldMEs Module eigengenes of the original modules in the sets given by useSets.

Module eigengenes of the merged modules in the sets given by useSets.

Module eigengenes of the merged modules in the sets given by useSets.

allOK A boolean set to TRUE.

If an error occurred and trapErrors==TRUE, the list only contains these components:

colors A copy of the input colors. allOK a boolean set to FALSE.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

metaAnalysis

Meta-analysis of binary and continuous variables

Description

This is a meta-analysis complement to functions standardScreeningBinaryTrait and standardScreeningNumericTrait Given expression (or other) data from multiple independent data sets, and the corresponding clinical traits or outcomes, the function calculates multiple screening statistics in each data set, then calculates meta-analysis Z scores, p-values, and optionally q-values (False Discovery Rates). Three different ways of calculating the meta-analysis Z scores are provided: the Stouffer method, weighted Stouffer method, and using user-specified weights.

Usage

Arguments

multiExpr Expression data (or other data) in multi-set format (see checkSets). A vector

of lists; in each list there must be a component named data whose content is a

matrix or dataframe or array of dimension 2.

multiTrait Trait or ourcome data in multi-set format. Only one trait is allowed; conseques-

ntly, the data component of each component list can be either a vector or a data

frame (matrix, array of dimension 2).

binary Logical: is the trait binary (TRUE) or continuous (FALSE)? If not given, the deci-

sion will be made based on the content of multiTrait.

metaAnalysisWeights

Optional specification of set weights for meta-analysis. If given, must be a vec-

tor of non-negative weights, one entry for each set contained in multiExpr.

corFnc Correlation function to be used for screening. Should be either the default cor

or its robust alternative, bicor.

corOptions A named list giving extra arguments to be passed to the correlation function.

getQvalues Logical: should q-values (FDRs) be calculated?

getAreaUnderROC

Logical: should area under the ROC be calculated? Caution, enabling the cal-

culation will slow the function down considerably for large data sets.

useRankPvalue Logical: should the rankPvalue function be used to obtain alternative meta-

analysis statistics?

rankPvalueOptions

Additional options for function rankPvalue. These include na.last (default "keep"), ties.method (default "average"), calculateQvalue (default copied

from input getQvalues), and pValueMethod (default "all"). See the help file

for rankPvalue for full details.

setNames Optional specification of set names (labels). These are used to label the corre-

sponding components of the output. If not given, will be taken from the names attribute of multiExpr. If names(multiExpr) is NULL, generic names of the

form Set_1, Set2, ... will be used.

kruskalTest Logical: should the Kruskal test be performed in addition to t-test? Only applies

to binary traits.

var.equal Logical: should the t-test assume equal variance in both groups? If TRUE, the

function will warn the user that the returned test statistics will be different from

the results of the standard t.test function.

metaKruskal Logical: should the meta-analysis be based on the results of Kruskal test (TRUE)

or Student t-test (FALSE)?

na.action Specification of what should happen to missing values in t.test.

Details

The Stouffer method of combines Z statistics by simply taking a mean of input Z statistics and multiplying it by sqrt(n), where n is the number of input data sets. We refer to this method as Stouffer.equalWeights. In general, a better (i.e., more powerful) method of combining Z

statistics is to weigh them by the number of degrees of freedom (which approximately equals n). We refer to this method as weightedStouffer. Finally, the user can also specify custom weights, for example if a data set needs to be downweighted due to technical concerns; however, specifying own weights by hand should be done carefully to avoid possible selection biases.

Value

Data frame with the following components:

ID Identifier of the input genes (or other variables)

Z. equalWeights Meta-analysis Z statistics obtained using Stouffer's method with equal weights

p.equalWeights p-values corresponding to Z.Stouffer.equalWeights

q.equalWeights q-values corresponding to p. Stouffer.equalWeights, only present if getQvalues

Z.RootDoFWeights

Meta-analysis Z statistics obtained using Stouffer's method with weights given by the square root of the number of (non-missing) samples in each data set

p.RootDoFWeights

p-values corresponding to Z.DoFWeights

q.RootDoFWeights

q-values corresponding to p.DoFWeights, only present if getQvalues is TRUE.

Z.DoFWeights Meta-analysis Z statistics obtained using Stouffer's method with weights given

by the number of (non-missing) samples in each data set

p.DoFWeights p-values corresponding to Z.DoFWeights

q.DoFWeights q-values corresponding to p.DoFWeights, only present if getQvalues is TRUE.

Z.userWeights Meta-analysis Z statistics obtained using Stouffer's method with user-defined

weights. Only present if input metaAnalysisWeights are present.

p.userWeights p-values corresponding to Z.userWeights

 ${\tt q.userWeights} \quad {\tt q-values} \ corresponding \ to \ {\tt p.userWeights}, only \ present \ if \ {\tt getQvalues} \ is \ {\tt TRUE}.$

The next set of columns is present only if input useRankPvalue is TRUE and contain the output of the function rankPvalue with the same column weights as the above meta-analysis. Depending on the input options calculateQvalue and pValueMethod in rankPvalueOptions, some columns may be missing. The following columns are calculated using equal weights for each data set.

pValueExtremeRank.equalWeights

This is the minimum between pValueLowRank and pValueHighRank, i.e. min(pValueLow, pValueHigh)

pValueLowRank.equalWeights

Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

pValueHighRank.equalWeights

Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

pValueExtremeScale.equalWeights

This is the minimum between pValueLowScale and pValueHighScale, i.e. min(pValueLow, pValueHigh)

pValueLowScale.equalWeights

Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method.

pValueHighScale.equalWeights

Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method.

qValueExtremeRank.equalWeights

local false discovery rate (q-value) corresponding to the p-value pValueExtremeR-ank

qValueLowRank.equalWeights

 $local\ false\ discovery\ rate\ (q\text{-}value)\ corresponding\ to\ the\ p\text{-}value\ pValueLowRank$

qValueHighRank.equalWeights

local false discovery rate (q-value) corresponding to the p-value pValueHigh-Rank

 ${\tt qValueExtremeScale.equalWeights}$

local false discovery rate (q-value) corresponding to the p-value pValueExtremeScale

qValueLowScale.equalWeights

local false discovery rate (q-value) corresponding to the p-value pValueLowS-cale

qValueHighScale.equalWeights

local false discovery rate (q-value) corresponding to the p-value pValueHigh-Scale

Analogous columns calculated by weighting each input set using the square root of the number of samples, number of samples, and user weights (if given). The corresponding column names carry the suffixes RootDofWeights, DoFWeights, userWeights.

The following columns contain results returned by standardScreeningBinaryTrait or standardScreeningNumericTrait (depending on whether the input trait is binary or continuous).

For binary traits, the following information is returned for each set:

```
corPearson.Set_1, corPearson.Set_2, ...
```

Pearson correlation with a binary numeric version of the input variable. The numeric variable equals 1 for level 1 and 2 for level 2. The levels are given by levels(factor(y)).

t.Student.Set_1, t.Student.Set_2, ...

Student t-test statistic

 $\verb|pvalueStudent.Set_1|, \verb|pvalueStudent.Set_2|, \dots$

two-sided Student t-test p-value.

qvalueStudent.Set_1, qvalueStudent.Set_2, ...

(if input qValues==TRUE) q-value (local false discovery rate) based on the Student T-test p-value (Storey et al 2004).

foldChange.Set_1, foldChange.Set_2, ...

a (signed) ratio of mean values. If the mean in the first group (corresponding to level 1) is larger than that of the second group, it equals meanFirst-Group/meanSecondGroup. But if the mean of the second group is larger than that of the first group it equals -meanSecondGroup/meanFirstGroup (notice the minus sign).

```
meanFirstGroup.Set_1, meanSecondGroup.Set_2, ...
                  means of columns in input datExpr across samples in the second group.
SE.FirstGroup.Set_1, SE.FirstGroup.Set_2, ...
                  standard errors of columns in input datExpr across samples in the first group.
                  Recall that SE(x)=\operatorname{sqrt}(\operatorname{var}(x)/n) where n is the number of non-missing values of
SE.SecondGroup.Set_1, SE.SecondGroup.Set_2, ...
                  standard errors of columns in input datExpr across samples in the second group.
areaUnderROC.Set_1, areaUnderROC.Set_2, ...
                  the area under the ROC, also known as the concordance index or C.index. This
                  is a measure of discriminatory power. The measure lies between 0 and 1 where
                  0.5 indicates no discriminatory power. 0 indicates that the "opposite" predictor
                  has perfect discriminatory power. To compute it we use the function rcorr.cens
                  with outx=TRUE (from Frank Harrel's package Hmisc).
nPresentSamples.Set_1, nPresentSamples.Set_2, ...
                  number of samples with finite measurements for each gene.
If input kruskalTest is TRUE, the following columns further summarize results of Kruskal-Wallis
test:
stat.Kruskal.Set_1, stat.Kruskal.Set_2, ...
                  Kruskal-Wallis test statistic.
stat.Kruskal.signed.Set_1, stat.Kruskal.signed.Set_2, ...
                  (Warning: experimental) Kruskal-Wallis test statistic including a sign that indi-
                  cates whether the average rank is higher in second group (positive) or first group
                  (negative).
pvaluekruskal.Set_1, pvaluekruskal.Set_2, ...
                  Kruskal-Wallis test p-value.
qkruskal.Set_1, qkruskal.Set_2, ...
                  q-values corresponding to the Kruskal-Wallis test p-value (if input qValues==TRUE).
Z. Set1, Z. Set2, . . .
                  Z statistics obtained from pvalueStudent.Set1, pvalueStudent.Set2, ...
                  or from pvaluekruskal.Set1, pvaluekruskal.Set2, ..., depending on in-
                  put metaKruskal.
For numeric traits, the following columns are returned:
cor.Set_1, cor.Set_2, ...
                  correlations of all genes with the trait
Z. Set1, Z. Set2, ...
                  Fisher Z statistics corresponding to the correlations
pvalueStudent.Set_1, pvalueStudent.Set_2, ...
                  Student p-values of the correlations
qvalueStudent.Set_1, qvalueStudent.Set_1, ...
                  (if input qValues==TRUE) q-values of the correlations calculated from the p-
                  values
AreaUnderROC.Set_1, AreaUnderROC.Set_2, ...
                  area under the ROC
nPresentSamples.Set_1, nPresentSamples.Set_2, ...
                  number of samples present for the calculation of each association.
```

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Author(s)

Peter Langfelder

References

For Stouffer's method, see

Stouffer, S.A., Suchman, E.A., DeVinney, L.C., Star, S.A. & Williams, R.M. Jr. 1949. The American Soldier, Vol. 1: Adjustment during Army Life. Princeton University Press, Princeton.

A discussion of weighted Stouffer's method can be found in

Whitlock, M. C., Combining probability from independent tests: the weighted Z-method is superior to Fisher's approach, Journal of Evolutionary Biology 18:5 1368 (2005)

See Also

standardScreeningBinaryTrait, standardScreeningNumericTrait for screening functions for individual data sets

metaZfunction

Meta-analysis Z statistic

Description

The function calculates a meta analysis Z statistic based on an input data frame of Z statistics.

Usage

metaZfunction(datZ, columnweights = NULL)

Arguments

datZ

Matrix or data frame of Z statistics (assuming standard normal distribution under the null hypothesis). Rows correspond to genes, columns to independent data

sets.

columnweights

optional vector of non-negative numbers for weighing the columns of datZ.

Details

For example, if datZ has 3 columns whose columns are labelled Z1,Z2,Z3 then ZMeta= (Z1+Z2+Z3)/sqrt(3). Under the null hypothesis (where all Z statistics follow a standard normal distribution and the Z statistics are independent), ZMeta also follows a standard normal distribution. To calculate a 2 sided p-value, one an use the following code pvalue=2*pnorm(-abs(ZMeta))

Value

Vector of meta analysis Z statistic. Under the null hypothesis this should follow a standard normal distribution.

minWhichMin 227

Author(s)

Steve Horvath

minWhichMin	Fast joint calculation of row- or column-wise minima and indices of minimum elements

Description

Fast joint calculation of row- or column-wise minima and indices of minimum elements. Missing data are removed.

Usage

```
minWhichMin(x, byRow = FALSE, dims = 1)
```

Arguments

v /		numeric	- 1	matriv	Or	arran
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byRow Logical: should the minima and indices be found for columns (FALSE) or rows

(TRUE)?

dims Specifies dimensions for which to find the minima and indices. For byRow =

FALSE, they are calculated for dimensions dims+1 to n=length(dim(x)); for

For byRow = TRUE, they are calculated for dimensions 1,...,dims.

Value

```
A list with two components, min and which; each is a vector or array with dimensions dim(x)[(dims+1):n] (with n=length(dim(x))) if byRow = FALSE, and
```

```
dim(x)[1:dims] if byRow = TRUE.
```

Author(s)

Peter Langfelder

modifiedBisquareWeights

Modified Bisquare Weights

Description

Calculation of bisquare weights and the intermediate weight factors similar to those used in the calculation of biweight midcovariance and midcorrelation. The weights are designed such that outliers get smaller weights; the weights become zero for data points more than 9 median absolute deviations from the median.

Usage

```
modifiedBisquareWeights(
    x,
    removedCovariates = NULL,
    pearsonFallback = TRUE,
    maxPOutliers = 0.05,
    outlierReferenceWeight = 0.1,
    groupsForMinWeightRestriction = NULL,
    minWeightInGroups = 0,
    maxPropUnderMinWeight = 1,
    defaultWeight = 1,
    getFactors = FALSE)
```

Arguments

Х

A matrix of numeric observations with variables (features) in columns and observations (samples) in rows. Weights will be calculated separately for each column.

removedCovariates

Optional matrix or data frame of variables that are to be regressed out of each column of x before calculating the weights. If given, must have the same number of rows as x.

pearsonFallback

Logical: for columns of x that have zero median absolute deviation (MAD), should the appropriately scaled standard deviation be used instead?

maxPOutliers

Optional numeric scalar between 0 and 1. Specifies the maximum proportion of outliers in each column, i.e., data with weights equal to outlierReferenceWeight below.

outlierReferenceWeight

A number between 0 and 1 specifying what is to be considered an outlier when calculating the proportion of outliers.

```
groupsForMinWeightRestriction
```

An optional vector with length equal to the number of samples (rows) in x giving a categorical variable. The output factors and weights are adjusted such that in

samples at each level of the variable, the weight is below minWeightInGroups in a fraction of samples that is at most maxPropUnderMinWeight.

minWeightInGroups

A threshold weight, see groupsForMinWeightRestriction and details.

maxPropUnderMinWeight

A proportion (number between 0 and 1). See groupsForMinWeightRestriction

and details.

defaultWeight Value used for weights that would be undefined or not finite, for example, when

a column in x is constant.

getFactors Logical: should the intermediate weight factors be returned as well?

Details

Weights are calculated independently for each column of x. Denoting a column of x as y, the weights are calculated as $(1-u^2)^2$ where u is defined as $\min(1,|y-m|/(9MMAD))$. Here m is the median of the column y and MMAD is the modified median absolute deviation. We call the expression |y-m|/(9MMAD) the weight factors. Note that outliers are observations with high (>1) weight factors for outliers but low (zero) weights.

The calculation of MMAD starts with calculating the (unscaled) median absolute deviation of the column x. If the median absolute deviation is zero and pearsonFallback is TRUE, it is replaced by the standard deviation (multiplied by qnorm(0.75) to make it asymptotically consistent with MAD). The following two conditions are then checked: (1) The proportion of weights below outlierReferenceWeight is at most maxPOutliers and (2) if groupsForMinWeightRestriction has non-zero length, then for each individual level in groupsForMinWeightRestriction, the proportion of samples with weights less than minWeightInGroups is at most maxPropUnderMinWeight. (If groupsForMinWeightRestriction is zero-length, the second condition is considered trivially satisfied.) If both conditions are met, MMAD equals the median absolute deviation, MAD. If either condition is not met, MMAD equals the lowest number for which both conditions are met.

Value

When the input getFactors is TRUE, a list with two components:

weights A matrix of the same dimensions and dimnames as the input x giving the weights

of the individual observations in x.

factors A matrix of the same form as weights giving the weight factors.

When the input getFactors is FALSE, the function returns the matrix of weights.

Author(s)

Peter Langfelder

References

A full description of the weight calculation can be found, e.g., in Methods section of

Wang N, Langfelder P, et al (2022) Mapping brain gene coexpression in daytime transcriptomes unveils diurnal molecular networks and deciphers perturbation gene signatures. Neuron. 2022 Oct 19;110(20):3318-3338.e9. PMID: 36265442; PMCID: PMC9665885. doi:10.1016/j.neuron.2022.09.028

Other references include, in reverse chronological order,

Peter Langfelder, Steve Horvath (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software, 46(11), 1-17. https://www.jstatsoft.org/v46/ill/

"Introduction to Robust Estimation and Hypothesis Testing", Rand Wilcox, Academic Press, 1997. "Data Analysis and Regression: A Second Course in Statistics", Mosteller and Tukey, Addison-Wesley, 1977, pp. 203-209.

See Also

bicovWeights for a simpler, less flexible calculation.

moduleColor.getMEprefix

Get the prefix used to label module eigengenes.

Description

Returns the currently used prefix used to label module eigengenes. When returning module eigengenes in a dataframe, names of the corresponding columns will start with the given prefix.

Usage

```
moduleColor.getMEprefix()
```

Details

Returns the prefix used to label module eigengenes. When returning module eigengenes in a dataframe, names of the corresponding columns will consist of the corresponfing color label preceded by the given prefix. For example, if the prefix is "PC" and the module is turquoise, the corresponding module eigengene will be labeled "PCturquoise". Most of old code assumes "PC", but "ME" is more instructive and used in some newer analyses.

Value

A character string.

Note

Currently the standard prefix is "ME" and there is no way to change it.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

See Also

moduleEigengenes

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moduleEigengenes	Calculate module eigengenes.

Description

Calculates module eigengenes (1st principal component) of modules in a given single dataset.

Usage

Arguments

6	
expr	Expression data for a single set in the form of a data frame where rows are samples and columns are genes (probes).
colors	A vector of the same length as the number of probes in expr, giving module color for all probes (genes). Color "grey" is reserved for unassigned genes.
impute	If TRUE, expression data will be checked for the presence of NA entries and if the latter are present, numerical data will be imputed, using function impute.knn and probes from the same module as the missing datum. The function impute.knn uses a fixed random seed giving repeatable results.
nPC	Number of principal components and variance explained entries to be calculated. Note that only the first principal component is returned; the rest are used only for the calculation of proportion of variance explained. The number of returned variance explained entries is currently min(nPC, 10). If given nPC is greater than 10, a warning is issued.
align	Controls whether eigengenes, whose orientation is undetermined, should be aligned with average expression (align = "along average", the default) or left as they are (align = ""). Any other value will trigger an error.
excludeGrey	Should the improper module consisting of 'grey' genes be excluded from the eigengenes?
grey	Value of colors designating the improper module. Note that if colors is a factor of numbers, the default value will be incorrect.

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subHubs Controls whether hub genes should be substituted for missing eigengenes. If

TRUE, each missing eigengene (i.e., eigengene whose calculation failed and the error was trapped) will be replaced by a weighted average of the most connected hub genes in the corresponding module. If this calculation fails, or if subHubs==FALSE, the value of trapErrors will determine whether the offending module will be removed or whether the function will issue an error and stop.

trapErrors Controls handling of errors from that may arise when there are too many NA

entries in expression data. If TRUE, errors from calling these functions will be trapped without abnormal exit. If FALSE, errors will cause the function to stop. Note, however, that subHubs takes precedence in the sense that if subHubs==TRUE and trapErrors==FALSE, an error will be issued only if both

the principal component and the hubgene calculations have failed.

returnValidOnlv

logical; controls whether the returned data frame of module eigengenes contains columns corresponding only to modules whose eigengenes or hub genes could be calculated correctly (TRUE), or whether the data frame should have columns

for each of the input color labels (FALSE).

softPower The power used in soft-thresholding the adjacency matrix. Only used when the

hubgene approximation is necessary because the principal component calculation failed. It must be non-negative. The default value should only be changed

if there is a clear indication that it leads to incorrect results.

scale logical; can be used to turn off scaling of the expression data before calculating

the singular value decomposition. The scaling should only be turned off if the data has been scaled previously, in which case the function can run a bit faster. Note however that the function first imputes, then scales the expression data in each module. If the expression contain missing data, scaling outside of the function and letting the function impute missing data may lead to slightly different

results than if the data is scaled within the function.

verbose Controls verbosity of printed progress messages. 0 means silent, up to (about) 5

the verbosity gradually increases.

indent A single non-negative integer controlling indentation of printed messages. 0

means no indentation, each unit above that adds two spaces.

Details

Module eigengene is defined as the first principal component of the expression matrix of the corresponding module. The calculation may fail if the expression data has too many missing entries. Handling of such errors is controlled by the arguments subHubs and trapErrors. If subHubs==TRUE, errors in principal component calculation will be trapped and a substitute calculation of hubgenes will be attempted. If this fails as well, behaviour depends on trapErrors: if TRUE, the offending module will be ignored and the return value will allow the user to remove the module from further analysis; if FALSE, the function will stop.

From the user's point of view, setting trapErrors=FALSE ensures that if the function returns normally, there will be a valid eigengene (principal component or hubgene) for each of the input colors. If the user sets trapErrors=TRUE, all calculational (but not input) errors will be trapped, but the user should check the output (see below) to make sure all modules have a valid returned eigengene.

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While the principal component calculation can fail even on relatively sound data (it does not take all that many "well-placed" NA to torpedo the calculation), it takes many more irregularities in the data for the hubgene calculation to fail. In fact such a failure signals there likely is something seriously wrong with the data.

Value

A list with the following components:

A list with the foli	owing components.
eigengenes	Module eigengenes in a dataframe, with each column corresponding to one eigengene. The columns are named by the corresponding color with an "ME" prepended, e.g., MEturquoise etc. If returnValidOnly==FALSE, module eigengenes whose calculation failed have all components set to NA.
averageExpr	If align == "along average", a dataframe containing average normalized expression in each module. The columns are named by the corresponding color with an "AE" prepended, e.g., AEturquoise etc.
varExplained	A dataframe in which each column corresponds to a module, with the component varExplained[PC, module] giving the variance of module module explained by the principal component no. PC. The calculation is exact irrespective of the number of computed principal components. At most 10 variance explained values are recorded in this dataframe.
nPC	A copy of the input nPC.
validMEs	A boolean vector. Each component (corresponding to the columns in data) is TRUE if the corresponding eigengene is valid, and FALSE if it is invalid. Valid eigengenes include both principal components and their hubgene approximations. When returnValidOnly==FALSE, by definition all returned eigengenes are valid and the entries of validMEs are all TRUE.
validColors	A copy of the input colors with entries corresponding to invalid modules set to grey if given, otherwise 0 if colors is numeric and "grey" otherwise.
allOK	Boolean flag signalling whether all eigengenes have been calculated correctly, either as principal components or as the hubgene average approximation.
allPC	Boolean flag signalling whether all returned eigengenes are principal components.
isPC	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding eigengene is the first principal component and FALSE if it is the hubgene approximation or is invalid.
isHub	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding eigengene is the hubgene approximation and FALSE if it is the first principal component or is invalid.
validAEs	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding module average expression is valid.
allAEOK	Boolean flag signalling whether all returned module average expressions contain valid data. Note that returnValidOnly==TRUE does not imply allAEOK==TRUE: some invalid average expressions may be returned if their corresponding eigengenes have been calculated correctly.

Author(s)

Steve Horvath <SHorvath@mednet.ucla.edu>, Peter Langfelder <Peter.Langfelder@gmail.com>

References

Zhang, B. and Horvath, S. (2005), "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

```
svd, impute.knn
```

moduleMergeUsingKME

Merge modules and reassign genes using kME.

Description

This function takes an expression data matrix (and other user-defined parameters), calculates the module membership (kME) values, and adjusts the module assignments, merging modules that are not sufficiently distinct and reassigning modules that were originally assigned suboptimally.

Usage

```
moduleMergeUsingKME(
  datExpr, colorh, ME = NULL,
  threshPercent = 50, mergePercent = 25,
  reassignModules = TRUE,
  convertGrey = TRUE,
  omitColors = "grey",
  reassignScale = 1,
  threshNumber = NULL)
```

Arguments

datExpr An expression data matrix, with samples as rows, genes (or probes) as column.

colorh The color vector (module assignments) corresponding to the columns of dat-

Expr.

ME Either NULL (default), at which point the module eigengenes will be calculated,

or pre-calculated module eigengenes for each of the modules, with samples as rows (corresponding to datExpr), and modules corresponding to columns (column names MUST be module colors or module colors prefixed by "ME" or

"PC").

threshPercent Threshold percent of the number of genes in the module that should be included

for the various analyses. For example, in a module with 200 genes, if threshPercent=50 (default), then 50 genes will be checked for reassignment and used to

test whether two modules should be merged. See also threshNumber.

mergePercent

If greater than this percent of the assigned genes are above the threshold are in a module other than the assigned module, then these two modules will be merged. For example, if mergePercent=25 (default), and the 70 out of 200 genes in the blue module were more highly correlated with the black module eigengene, then all genes in the blue module would be reassigned to the black module.

reassignModules

If TRUE (default), genes are resassigned to the module with which they have the highest module membership (kME), but only if their kME is above the thresh-Percent (or threshNumber) threshold of that module.

convertGrey If TRUE (default), unassigned (grey) genes are assigned as in "reassignMod-

ules"

omitColors These are all of the module assignments which indicate genes that are not as-

signed to modules (default="grey"). These genes will all be assigned as "grey"

by this function.

reassignScale A value between 0 and 1 (default) which determines how the threshPercent gets

scaled for reassigning genes. Smaller values reassign more genes, but does not

affect the merging process.

threshNumber Either NULL (default) or, if entered, every module is counted as having exactly

threshNumber genes, and threshPercent it ignored. This parameter should have

the effect of

Value

moduleColors The NEW color vector (module assignments) corresponding to the columns of

datExpr, after module merging and reassignments.

mergeLog A log of the order in which modules were merged, for reference.

Note

Note that this function should be considered "experimental" as it has only been beta tested. Please e-mail jeremyinla@gmail.com if you have any issues with the function.

Author(s)

Jeremy Miller

Examples

```
## First simulate some data and the resulting network dendrogram
set.seed(100)
MEturquoise = sample(1:100,50)
          = sample(1:100,50)
MEblue
MEbrown
           = sample(1:100,50)
MEyellow = sample(1:100,50)
           = c(MEyellow[1:30], sample(1:100,20))
MEgreen
MEred
         = c(MEbrown [1:20], sample(1:100,30))
#MEblack
            = c(MEblue [1:25], sample(1:100,25))
ME = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen, MEred)#, MEblack)
dat1 = simulateDatExpr(ME, 300, c(0.15,0.13,0.12,0.10,0.09,0.09,0.1), signed=TRUE)
```

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```
TOM1 = TOMsimilarityFromExpr(dat1$datExpr, networkType="signed", nThreads = 1)
tree1 = fastcluster::hclust(as.dist(1-TOM1),method="average")
## Here is an example using different mergePercentages,
# setting an inclusive threshPercent (91)
colorh1 <- colorPlot <- labels2colors(dat1$allLabels)</pre>
merges = c(65, 40, 20, 5)
for (m in merges)
  colorPlot = cbind(colorPlot,
                     moduleMergeUsingKME(dat1$datExpr,colorh1,
                        threshPercent=91, mergePercent=m)$moduleColors)
plotDendroAndColors(tree1, colorPlot, c("ORIG", merges), dendroLabels=FALSE)
## Here is an example using a lower reassignScale (so that more genes get reassigned)
colorh1 <- colorPlot <- labels2colors(dat1$allLabels)</pre>
merges = c(65, 40, 20, 5)
for (m in merges) colorPlot = cbind(colorPlot,
 moduleMergeUsingKME(dat1$datExpr,colorh1,threshPercent=91,
                      reassignScale=0.7, mergePercent=m)$moduleColors)
plotDendroAndColors(tree1, colorPlot, c("ORIG",merges), dendroLabels=FALSE)
## Here is an example using a less-inclusive threshPercent (75),
# little if anything is merged.
colorh1 <- colorPlot <- labels2colors(dat1$allLabels)</pre>
merges = c(65, 40, 20, 5)
for (m in merges) colorPlot = cbind(colorPlot,
 moduleMergeUsingKME(dat1$datExpr,colorh1,
                      threshPercent=75, mergePercent=m)$moduleColors)
plotDendroAndColors(tree1, colorPlot, c("ORIG",merges), dendroLabels=FALSE)
# (Note that with real data, the default threshPercent=50 usually results
# in some modules being merged)
```

moduleNumber

Fixed-height cut of a dendrogram.

Description

Detects branches of on the input dendrogram by performing a fixed-height cut.

Usage

```
moduleNumber(dendro, cutHeight = 0.9, minSize = 50)
```

Arguments

dendro a hierarchical clustering dendorgram such as one returned by hclust.

cutHeight Maximum joining heights that will be considered.

minSize Minimum cluster size.

Details

All contiguous branches below the height cutHeight that contain at least minSize objects are assigned unique positive numerical labels; all unassigned objects are assigned label 0.

Value

A vector of numerical labels giving the assignment of each object.

Note

The numerical labels may not be sequential. See normalizeLabels for a way to put the labels into a standard order.

Author(s)

```
Peter Langfelder, <Peter.Langfelder@gmail.com>
```

See Also

```
hclust, cutree, normalizeLabels
```

modulePreservation

Calculation of module preservation statistics

Description

Calculations of module preservation statistics between independent data sets.

Usage

```
modulePreservation(
   multiData,
   multiColor,
   multiWeights = NULL,
   dataIsExpr = TRUE,
   networkType = "unsigned",
   corFnc = "cor",
   corOptions = "use = 'p'",
   referenceNetworks = 1,
   testNetworks = NULL,
   nPermutations = 100,
   includekMEallInSummary = FALSE,
   restrictSummaryForGeneralNetworks = TRUE,
   calculateQvalue = FALSE,
   randomSeed = 12345,
   maxGoldModuleSize = 1000,
   maxModuleSize = 1000,
```

```
quickCor = 1,
ccTupletSize = 2,
calculateCor.kIMall = FALSE,
calculateClusterCoeff = FALSE,
useInterpolation = FALSE,
checkData = TRUE,
greyName = NULL,
goldName = NULL,
savePermutedStatistics = TRUE,
loadPermutedStatistics = FALSE,
permutedStatisticsFile = if (useInterpolation) "permutedStats-intrModules.RData"
                                 else "permutedStats-actualModules.RData",
plotInterpolation = TRUE,
interpolationPlotFile = "modulePreservationInterpolationPlots.pdf",
discardInvalidOutput = TRUE,
parallelCalculation = FALSE,
verbose = 1, indent = 0)
```

Arguments

multiData

expression data or adjacency data in multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression or adjacency data. If expression data are used, rows correspond to samples and columns to genes or probes. In case of adjacencies, each data matrix should be a symmetric matrix ith entries between 0 and 1 and unit diagonal. Each component of the outermost list should be named.

multiColor

a list in which every component is a vector giving the module labels of genes in multiExpr. The components must be named using the same names that are used in multiExpr; these names are used top match labels to expression data sets. See details.

multiWeights

optional weights, only when multiData contains expression data. If given, must be in the multi-set format (see checkSets) and weights for each set must have the same dimensions as the corresponding set in multiData. The weights are used in correlation calculations that involve multiData, and are supplied as argument weights.x and possibly weights.y (where appropriate) to the correlation function specified by corFnc.

dataIsExpr

logical: if TRUE, multiData will be interpreted as expression data; if FALSE, multiData will be interpreted as adjacencies.

networkType

network type. Allowed values are (unique abbreviations of) "unsigned", "signed", "signed hybrid". See adjacency.

corFnc

character string specifying the function to be used to calculate co-expression similarity. Defaults to Pearson correlation. Another useful choice is bicor. More generally, any function returning values between -1 and 1 can be used.

corOptions

character string specifying additional arguments to be passed to the function given by corFnc. Use "use = 'p', method = 'spearman'" to obtain Spearman correlation.

referenceNetworks

a vector giving the indices of expression data to be used as reference networks. Reference networks must have their module labels given in multiColor.

testNetworks

a list with one component per each entry in referenceNetworks above, giving the test networks in which to evaluate module preservation for the corresponding reference network. If not given, preservation will be evaluated in all networks (except each reference network). If referenceNetworks is of length 1, testNetworks can also be a vector (instead of a list containing the single vector).

nPermutations

specifies the number of permutations that will be calculated in the permutation test

includekMEallInSummary

logical: should cor.kMEall be included in the calculated summary statistics? Because kMEall takes into account all genes in the network, this statistic measures preservation of the full network with respect to the eigengene of the module. This may be undesirable, hence the default is FALSE.

restrictSummaryForGeneralNetworks

logical: should the summary statistics for general (not correlation) networks be restricted (density to meanAdj, connectivity to cor.kIM and cor.Adj)? The default TRUE corresponds to published work.

calculateQvalue

logical: should q-values (local FDR estimates) be calculated? Package qvalue must be installed for this calculation. Note that q-values may not be meaningful when the number of modules is small and/or most modules are preserved.

randomSeed

seed for the random number generator. If NULL, the seed will not be set. If non-NULL and the random generator has been initialized prior to the function call, the latter's state is saved and restored upon exit

maxGoldModuleSize

maximum size of the "gold" module, i.e., the random sample of all network genes.

maxModuleSize

maximum module size used for calculations. Modules larger than maxModuleSize will be reduced by randomly sampling maxModuleSize genes.

quickCor

number between 0 and 1 specifying the handling of missing data in calculation of correlation. Zero means exact but potentially slower calculations; one means potentially faster calculations, but with potentially inaccurate results if the proportion of missing data is large. See cor for more details.

ccTupletSize

tuplet size for co-clustering calculations.

calculateCor.kIMall

logical: should cor.kMEall be calculated? This option is only valid for adjacency input. If FALSE, cor.kIMall will not be calculated, potentially saving significant amount of time if the input adjacencies are large and contain many modules.

calculateClusterCoeff

logical: should statistics based on the clustering coefficient be calculated? While these statistics may be interesting, the calculations are also computationally expensive.

checkData logical: should data be checked for excessive number of missing entries? See

goodSamplesGenesMS for details.

greyName label used for unassigned genes. Traditionally such genes are labeled by grey

color or numeric label 0. These values are the default when ${\tt multiColor}$ con-

tains character or numeric vectors, respectively.

goldName label used for the "module" representing a random sample of the whole network.

Traditionally such genes are labeled by gold color or numeric label 0.1. These values are the default when greyName is character and numeric, respectively. If these values conflict with the module labels in multiColor, they should be set

to something not present in multiColor.

savePermutedStatistics

logical: should calculated permutation statistics be saved? Saved statistics may be re-used if the calculation needs to be repeated.

permutedStatisticsFile

file name to save the permutation statistics into.

loadPermutedStatistics

logical: should permutation statistics be loaded? If a previously executed calculation needs to be repeated, loading permutation study results can cut the calculation study results can

lation time many-fold.

useInterpolation

logical: should permutation statistics be calculated by interpolating an artificial set of evenly spaced modules? This option may potentially speed up the calculations, but it restricts calculations to density measures.

plotInterpolation

logical: should interpolation plots be saved? If interpolation is used (see useInterpolation above), the function can optionally generate diagnostic plots that can be used to assess whether the interpolation makes sense.

interpolationPlotFile

file name to save the interpolation plots into.

discardInvalidOutput

logical: should output columns containing no valid data be discarded? This option may be useful when input dataIsExpr is FALSE and some of the output statistics cannot be calculated. This option causes such statistics to be dropped from output.

parallelCalculation

logical: should calculations be done in parallel? Note that parallel calculations are turned off by default and will lead to somewhat DIFFERENT results than serial calculations because the random seed is set differently. For the calculation to actually run in parallel mode, a call to enableWGCNAThreads must be made

before this function is called.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

This function calculates module preservation statistics pair-wise between given reference sets and all other sets in multiExpr. Reference sets must have their corresponding module assignment specified in multiColor; module assignment is optional for test sets. Individual expression sets and their module labels are matched using names of the corresponding components in multiExpr and multiColor.

For each reference-test pair, the function calculates module preservation statistics that measure how well the modules of the reference set are preserved in the test set. If the multiColor also contains module assignment for the test set, the calculated statistics also include cross-tabulation statistics that make use of the test module assignment.

For each reference-test pair, the function only uses genes (columns of the data component of each component of multiExpr) that are in common between the reference and test set. Columns are matched by column names, so column names must be valid.

In addition to preservation statistics, the function also calculates several statistics of module quality, that is measures of how well-defined modules are in the reference set. The quality statistics are calculated with respect to genes in common with with a test set; thus the function calculates a set of quality statistics for each reference-test pair. This may be somewhat counter-intuitive, but it allows a direct comparison of corresponding quality and preservation statistics.

The calculated p-values are determined from the Z scores of individual measures under assumption of normality. No p-value is calculated for the Zsummary measures. Bonferoni correction to the number of tested modules. Because the p-values for strongly preserved modules are often extremely low, the function reports natural logarithms (base e) of the p-values. However, q-values are reported untransformed since they are calculated that way in package qvalue.

Missing data are removed (but see quickCor above).

Value

The function returns a nested list of preservation statistics. At the top level, the list components are:

quality observed values, Z scores, log p-values, Bonferoni-corrected log p-values, and

(optionally) q-values of quality statistics. All logarithms are in base 10.

observed values, Z scores, log p-values, Bonferoni-corrected log p-values, and (optionally) q-values of density and connectivity preservation statistics. All log-

arithms are in base 10.

accuracy observed values, Z scores, log p-values, Bonferoni-corrected log p-values, and

(optionally) q-values of cross-tabulation statistics. All logarithms are in base 10.

referenceSeparability

observed values, Z scores, log p-values, Bonferoni-corrected log p-values, and (optionally) q-values of module separability in the reference network. All logarithms are in base 10.

testSeparability

preservation

observed values, Z scores, p-values, Bonferoni-corrected p-values, and (optionally) q-values of module separability in the test network. All logarithms are in base 10.

permutationDetails

results of individual permutations, useful for diagnostics

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All of the above are lists. The lists quality, preservation, referenceSeparability, and testSeparability each contain 4 or 5 components: observed contains observed values, Z contains the corresponding Z scores, log.p contains base 10 logarithms of the p-values, log.pBonf contains base 10 logarithms of the Bonferoni corrected p-values, and optionally q contains the associated q-values. The list accuracy contains observed, Z, log.p, log.pBonf, optionally q, and additional components observedOverlapCounts and observedFisherPvalues that contain the observed matrices of overlap counts and Fisher test p-values.

Each of the lists observed, Z, log.p, log.pBonf, optionally q, observedOverlapCounts and observedFisherPvalues is structured as a 2-level list where the outer components correspond to reference sets and the inner components to tests sets. As an example, preservation\$observed[[1]][[2]] contains the density and connectivity preservation statistics for the preservation of set 1 modules in set 2, that is set 1 is the reference set and set 2 is the test set. preservation\$observed[[1]][[2]] is a data frame in which each row corresponds to a module in the reference network 1 plus one row for the unassigned objects, and one row for a "module" that contains randomly sampled objects and that represents a whole-network average. Each column corresponds to a statistic as indicated by the column name.

Note

For large data sets, the permutation study may take a while (typically on the order of several hours). Use verbose = 3 to get detailed progress report as the calculations advance.

Author(s)

Rui Luo and Peter Langfelder

References

Peter Langfelder, Rui Luo, Michael C. Oldham, and Steve Horvath, to appear

See Also

Network construction and module detection functions in the WGCNA package such as adjacency, blockwiseModules; rudimentary cleaning in goodSamplesGenesMS; the WGCNA implementation of correlation in cor.

mtd.apply

Apply a function to each set in a multiData structure.

Description

Inspired by lapply, these functions apply a given function to each data component in the input multiData structure, and optionally simplify the result to an array if possible.

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Usage

```
mtd.apply(
   # What to do
   multiData, FUN, ...,
   # Pre-existing results and update options
   mdaExistingResults = NULL, mdaUpdateIndex = NULL,
   mdaCopyNonData = FALSE,
   # Output formatting options
   mdaSimplify = FALSE,
   returnList = FALSE,
   # Internal behaviour options
   mdaVerbose = 0, mdaIndent = 0)
mtd.applyToSubset(
   # What to do
   multiData, FUN, ...,
   # Which rows and cols to keep
   mdaRowIndex = NULL, mdaColIndex = NULL,
   # Pre-existing results and update options
   mdaExistingResults = NULL, mdaUpdateIndex = NULL,
   mdaCopyNonData = FALSE,
    # Output formatting options
   mdaSimplify = FALSE,
   returnList = FALSE,
   # Internal behaviour options
   mdaVerbose = 0, mdaIndent = 0)
```

Arguments

multiData A multiData structure to apply the function over

FUN Function to be applied.

. . . Other arguments to the function FUN.

mdaRowIndex If given, must be a list of the same length as multiData. Each element must be

a logical or numeric vector that specifies rows in each data component to select

before applying the function.

mdaColIndex A logical or numeric vector that specifies columns in each data component to

select before applying the function.

mdaExistingResults

Optional list that contains previously calculated results. This can be useful if

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> only a few sets in multiData have changed and recalculating the unchanged ones is computationally expensive. If not given, all calculations will be performed. If given, components of this list are copied into the output. See mdmUpdateIndex for which components are re-calculated by default.

mdaUpdateIndex

Optional specification of which sets in multiData the calculation should actually be carried out. This argument has an effect only if mdaExistingResults is non-NULL. If the length of mdaExistingResults (call the length 'k') is less than the number of sets in multiData, the function assumes that the existing results correspond to the first 'k' sets in multiData and the rest of the sets are automatically calculated, irrespective of the setting of mdaUpdateIndex. The argument mdaUpdateIndex can be used to specify re-calculation of some (or all) of the results that already exist in mdaExistingResults.

mdaCopyNonData Logical: should non-data components of multiData be copied into the output? Note that the copying is incompatible with simplification; enabling both will trigger an error.

mdaSimplify

Logical: should the result be simplified to an array, if possible? Note that this may lead to errors; if so, disable simplification.

returnList

Logical: should the result be turned into a list (rather than a multiData structure)? Note that this is incompatible with simplification: if mdaSimplify is TRUE, this argument is ignored.

mdaVerbose

Integer specifying whether progress diagnistics should be printed out. Zero means silent, increasing values will lead to more diagnostic messages.

mdaIndent

Integer specifying the indentation of the printed progress messages. Each unit equals two spaces.

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

mtd.apply works on any "loose" multiData structure; mtd.applyToSubset assumes (and checks for) a "strict" multiData structure.

Value

A multiData structure containing the results of the supplied function on each data component in the input multiData structure. Other components are simply copied.

Author(s)

Peter Langfelder

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See Also

multiData to create a multiData structure; mtd.applyToSubset for applying a function to a subset of a multiData structure; mtd.mapply for vectorizing over several arguments.

mtd.mapply

Apply a function to elements of given multiData structures.

Description

Inspired by mapply, this function applies a given function to each data component in the input multiData arguments, and optionally simplify the result to an array if possible.

Usage

```
mtd.mapply(
    # What to do
    FUN, ..., MoreArgs = NULL,

# How to interpret the input
    mdma.argIsMultiData = NULL,

# Copy previously known results?
    mdmaExistingResults = NULL, mdmaUpdateIndex = NULL,

# How to format output
    mdmaSimplify = FALSE,
    returnList = FALSE,

# Options controlling internal behaviour
    mdma.doCollectGarbage = FALSE,
    mdmaVerbose = 0, mdmaIndent = 0)
```

Arguments

FUN Function to be applied.

... Arguments to be vectorized over. These can be multiData structures or simple

vectors (e.g., lists).

MoreArgs A named list that specifies the scalar arguments (if any) to FUN.

mdma.argIsMultiData

Optional specification whether arguments are multiData structures. A logical vector where each component corresponds to one entry of If not given, multiData status will be determined using isMultiData with argument strict=FALSE.

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mdmaExistingResults

Optional list that contains previously calculated results. This can be useful if only a few sets in multiData have changed and recalculating the unchanged ones is computationally expensive. If not given, all calculations will be performed. If given, components of this list are copied into the output. See mdmUpdateIndex for which components are re-calculated by default.

mdmaUpdateIndex

Optional specification of which sets in multiData the calculation should actually be carried out. This argument has an effect only if mdmaExistingResults is non-NULL. If the length of mdmaExistingResults (call the length 'k') is less than the number of sets in multiData, the function assumes that the existing results correspond to the first 'k' sets in multiData and the rest of the sets are automatically calculated, irrespective of the setting of mdmaUpdateIndex. The argument mdmaUpdateIndex can be used to specify re-calculation of some (or all) of the results that already exist in mdmaExistingResults.

mdmaSimplify Logical: should simplification of the result to an array be attempted? The sim-

plification is fragile and can produce unexpected errors; use the default FALSE if

that happens.

returnList Logical: should the result be turned into a list (rather than a multiData struc-

ture)? Note that this is incompatible with simplification: if mdaSimplify is

TRUE, this argument is ignored.

mdma.doCollectGarbage

Should garbage collection be forced after each application of FUN?

mdmaVerbose Integer specifying whether progress diagnistics should be printed out. Zero

means silent, increasing values will lead to more diagnostic messages.

mdmaIndent Integer specifying the indentation of the printed progress messages. Each unit

equals two spaces.

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

This function applies the function FUN to each data component of those arguments in . . . that are multiData structures in the "loose" sense, and to each component of those arguments in . . . that are not multiData structures.

Value

A multiData structure containing (as the data components) the results of FUN. If simplification is successful, an array instead.

mtd.rbindSelf 247

Author(s)

Peter Langfelder

See Also

multiData to create a multiData structure;
multiData.apply for application of a function to a single multiData structure.

mtd.rbindSelf

Turn a multiData structure into a single matrix or data frame.

Description

This function "rbinds" the data components of all sets in the input into a single matrix or data frame.

Usage

```
mtd.rbindSelf(multiData)
```

Arguments

multiData

A multiData structure.

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

This function requires a "strict" multiData structure.

Value

A single matrix or data frame containing the "rbinded" result.

Author(s)

Peter Langfelder

See Also

```
multiData to create a multiData structure;
```

rbind for various subtleties of the row binding operation.

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mtd.setAttr

Set attributes on each component of a multiData structure

Description

Set attributes on each data component of a multiData structure

Usage

```
mtd.setAttr(multiData, attribute, valueList)
```

Arguments

multiData A multiData structure.

attribute Name for the attribute to be set

valueList List that gives the attribute value for each set in the multiData structure.

Value

The input multiData with the attribute set on each data component.

Author(s)

Peter Langfelder

See Also

```
multiData to create a multiData structure;
```

isMultiData for a description of the multiData structure.

mtd.setColnames

Get and set column names in a multiData structure.

Description

Get and set column names on each data component in a multiData structure.

Usage

```
mtd.colnames(multiData)
mtd.setColnames(multiData, colnames)
```

Arguments

multiData A multiData structure

colnames A vector (coercible to character) of column names.

mtd.simplify 249

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

The mtd.colnames and mtd.setColnames assume (and checks for) a "strict" multiData structure.

Value

mtd.colnames returns the vector of column names of the data component. The function assumes the column names in all sets are the same.

mtd.setColnames returns the multiData structure with the column names set in all data components.

Author(s)

Peter Langfelder

See Also

multiData to create a multiData structure.

mtd.simplify

If possible, simplify a multiData structure to a 3-dimensional array.

Description

This function attempts to put all data components into a 3-dimensional array, with the last dimension corresponding to the sets. This is only possible if all data components are matrices or data frames with the same dimensions.

Usage

```
mtd.simplify(multiData)
```

Arguments

multiData

A multiData structure in the "strict" sense (see below).

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Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

This function assumes a "strict" multiData structure.

Value

A 3-dimensional array collecting all data components.

Note

The function is relatively fragile and may fail. Use at your own risk.

Author(s)

Peter Langfelder

See Also

```
multiData to create a multiData structure;
multiData2list for converting multiData structures to plain lists.
```

mtd.subset

Subset rows and columns in a multiData structure

Description

The function restricts each data component to the given columns and rows.

Usage

```
mtd.subset(
    # Input
    multiData,

# Rows and columns to keep
    rowIndex = NULL, colIndex = NULL,
    invert = FALSE,

# Strict or permissive checking of structure?
    permissive = FALSE,
```

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```
# Output formatting options
drop = FALSE)
```

Arguments

multiData A multiData structure.

rowIndex A list in which each component corresponds to a set and is a vector giving the

rows to be retained in that set. All indexing methods recognized by R can be used (numeric, logical, negative indexing, etc). If NULL, all columns will be retained in each set. Note that setting individual elements of rowIndex to NULL

will lead to errors.

colIndex A vector giving the columns to be retained. All indexing methods recognized

by R can be used (numeric, logical, negative indexing, etc). In addition, column names of the retained columns may be given; if a given name cannot be matched to a column, an error will be thrown. If NULL, all columns will be retained.

invert Logical: should the selection be inverted?

permissive Logical: should the function tolerate "loose" multiData input? Note that the

subsetting may lead to cryptic errors if the input multiData does not follow the

"strict" format.

drop Logical: should dimensions with extent 1 be dropped?

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

This function assumes a "strict" multiData structure unless permissive is TRUE.

Value

A multiData structure containing the selected rows and columns. Attributes (except possibly dimensions and the corresponding dimnames) are retained.

Author(s)

Peter Langfelder

See Also

multiData to create a multiData structure.

252 multiData

multiData

Create a multiData structure.

Description

This function creates a multiData structure by storing its input arguments as the 'data' components.

Usage

```
multiData(...)
```

Arguments

Arguments to be stored in the multiData structure.

Details

A multiData structure is intended to store (the same type of) data for multiple, possibly independent, realizations (for example, expression data for several independent experiments). It is a list where each component corresponds to an (independent) data set. Each component is in turn a list that can hold various types of information but must have a data component. In a "strict" multiData structure, the data components are required to each be a matrix or a data frame and have the same number of columns. In a "loose" multiData structure, the data components can be anything (but for most purposes should be of comparable type and content).

Value

The resulting multiData structure.

Author(s)

Peter Langfelder

See Also

multiData2list for converting a multiData structure to a list; list2multiData for an alternative way of creating a multiData structure; mtd.apply, mtd.applyToSubset, mtd.mapply for ways of applying a function to each component of a multiData structure.

Examples

```
data1 = matrix(rnorm(100), 20, 5);
data2 = matrix(rnorm(50), 10, 5);
md = multiData(Set1 = data1, Set2 = data2);
checkSets(md)
```

```
multiData.eigengeneSignificance
```

Eigengene significance across multiple sets

Description

This function calculates eigengene significance and the associated significance statistics (p-values, q-values etc) across several data sets.

Usage

```
multiData.eigengeneSignificance(
   multiData, multiTrait,
   moduleLabels, multiEigengenes = NULL,
   useModules = NULL,
   corAndPvalueFnc = corAndPvalue, corOptions = list(),
   corComponent = "cor",
   getQvalues = FALSE, setNames = NULL,
   excludeGrey = TRUE, greyLabel = ifelse(is.numeric(moduleLabels), 0, "grey"))
```

Arguments

multiData	Expression data (or other data) in multi-set format (see checkSets). A vector
	of lists; in each list there must be a component named data whose content is a
	matrix or dataframe or array of dimension 2.
multiTrait	Trait or ourcome data in multi-set format. Only one trait is allowed: conseques-

ntly, the data component of each component list can be either a vector or a data frame (matrix, array of dimension 2).

moduleLabels Module labels: one label for each gene in multiExpr.

multiEigengenes

Optional eigengenes of modules specified in moduleLabels. If not given, will

be calculated from ${\tt multiExpr.}$

useModules Optional specification of module labels to which the analysis should be re-

stricted. This could be useful if there are many modules, most of which are not interesting. Note that the "grey" module cannot be used with useModules.

corAndPvalueFnc

Function that calculates associations between expression profiles and eigen-

genes. See details.

corOptions List giving additional arguments to function corAndPvalueFnc. See details.

corComponent Name of the component of output of corAndPvalueFnc that contains the actual

correlation.

getQvalues logical: should q-values (estimates of FDR) be calculated?

setNames names for the input sets. If not given, will be taken from names(multiExpr). If

those are NULL as well, the names will be "Set_1", "Set_2",

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excludeGrey logical: should the grey module be excluded from the kME tables? Since the

grey module is typically not a real module, it makes little sense to report kME

values for it.

greyLabel label that labels the grey module.

Details

This is a convenience function that calculates module eigengene significances (i.e., correlations of module eigengenes with a given trait) across all sets in a multi-set analysis. Also returned are p-values, Z scores, numbers of present (i.e., non-missing) observations for each significance, and optionally the q-values (false discovery rates) corresponding to the p-values.

The function corAndPvalueFnc is currently is expected to accept arguments x (gene expression profiles) and y (eigengene expression profiles). Any additional arguments can be passed via corOptions.

The function corAndPvalueFnc should return a list which at the least contains (1) a matrix of associations of genes and eigengenes (this component should have the name given by corComponent), and (2) a matrix of the corresponding p-values, named "p" or "p.value". Other components are optional but for full functionality should include (3) n0bs giving the number of observations for each association (which is the number of samples less number of missing data - this can in principle vary from association to association), and (4) Z giving a Z static for each observation. If these are missing, n0bs is calculated in the main function, and calculations using the Z statistic are skipped.

Value

A list containing the following components. Each component is a matrix in which the rows correspond to module eigengenes and columns to data sets. Row and column names are set appropriately.

eigengeneSignificance

Module eigengene significance.

p.value p-values (returned by corAndPvalueFnc).

q.value q-values corresponding to the p-values above. Only returned in input getWvalues

is TRUE.

Z statistics (if returned by corAndPvalueFnc).

nObservations Number of non-missing observations in each correlation/p-value.

Author(s)

Peter Langfelder

multiGSub Analogs of grep(l) and (g) sub for multiple patterns and relacements

Description

These functions provide convenient pattern finding and substitution for multiple patterns.

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Usage

```
multiGSub(patterns, replacements, x, ...)
multiSub(patterns, replacements, x, ...)
multiGrep(patterns, x, ..., sort = TRUE, value = FALSE, invert = FALSE)
multiGrep1(patterns, x, ...)
```

Arguments

patterns	A character vector of patterns.
replacements	A character vector of replacements; must be of the same length as patterns.
X	Character vector of strings in which the pattern finding and replacements should be carried out.
sort	Logical: should the output indices be sorted in increasing order?
value	Logical: should value rather than the index of the value be returned?
invert	Logical: should the search be inverted and only indices of elements of x matching none of the patterns be returned?
	Other arguments to sub or grep

Details

For each element of x, patterns are sequentiall searched for and (for multiSub and multiGSub substituted with the corresponding replacement.

Value

multiSub and multiGSub return a character vector of the same length as x, with all patterns replaces by their replacements in each element of x. multiSub replaces each pattern in each element of x only once, multiGSub as many times as the pattern is found.

multiGrep returns the indices of those elements in x in which at least one of patterns was found, or, if invert is TRUE, the indices of elements in which none of the patterns were found. If value is TRUE, values rather than indices are returned.

multiGrepl returns a logical vector of the same length as x, with TRUE is any of the patterns matched the element of x, and FALSE otherwise.

Author(s)

Peter Langfelder

See Also

The workhorse functions sub, gsub, grep and grep1.

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multiSetMEs

Calculate module eigengenes.

Description

Calculates module eigengenes for several sets.

Usage

```
multiSetMEs(exprData,
            colors,
            universalColors = NULL,
            useSets = NULL,
            useGenes = NULL,
            impute = TRUE,
            nPC = 1,
            align = "along average",
            excludeGrey = FALSE,
            grey = if (is.null(universalColors)) {
                       if (is.numeric(colors)) 0 else "grey"
                   } else
                       if (is.numeric(universalColors)) 0 else "grey",
            subHubs = TRUE,
            trapErrors = FALSE,
            returnValidOnly = trapErrors,
            softPower = 6,
            verbose = 1, indent = 0)
```

Arguments

exprData

Expression data in a multi-set format (see checkSets). A vector of lists, with each list corresponding to one microarray dataset and expression data in the component data, that is expr[[set]]\$data[sample, probe] is the expression of probe probe in sample sample in dataset set. The number of samples can be different between the sets, but the probes must be the same.

colors

A matrix of dimensions (number of probes, number of sets) giving the module assignment of each gene in each set. The color "grey" is interpreted as unassigned.

universalColors

Alternative specification of module assignment. A single vector of length (number of probes) giving the module assignment of each gene in all sets (that is the modules are common to all sets). If given, takes precedence over color.

useSets

If calculations are requested in (a) selected set(s) only, the set(s) can be specified here. Defaults to all sets.

useGenes

Can be used to restrict calculation to a subset of genes (the same subset in all sets). If given, validColors in the returned list will only contain colors for the genes specified in useGenes.

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impute Logical. If TRUE, expression data will be checked for the presence of NA entries and if the latter are present, numerical data will be imputed, using function

impute.knn and probes from the same module as the missing datum. The function impute.knn uses a fixed random seed giving repeatable results.

nPC. Number of principal components to be calculated. If only eigengenes are needed,

it is best to set it to 1 (default). If variance explained is needed as well, use value NULL. This will cause all principal components to be computed, which is slower.

Controls whether eigengenes, whose orientation is undetermined, should be align

aligned with average expression (align = "along average", the default) or left

as they are (align = ""). Any other value will trigger an error.

excludeGrey Should the improper module consisting of 'grey' genes be excluded from the

eigengenes?

Value of colors or universalColors (whichever applies) designating the imgrey

proper module. Note that if the appropriate colors argument is a factor of num-

bers, the default value will be incorrect.

subHubs Controls whether hub genes should be substituted for missing eigengenes. If

TRUE, each missing eigengene (i.e., eigengene whose calculation failed and the error was trapped) will be replaced by a weighted average of the most connected hub genes in the corresponding module. If this calculation fails, or if subHubs==FALSE, the value of trapErrors will determine whether the offending module will be removed or whether the function will issue an error and stop.

trapErrors Controls handling of errors from that may arise when there are too many NA

entries in expression data. If TRUE, errors from calling these functions will be trapped without abnormal exit. If FALSE, errors will cause the function to stop. Note, however, that subHubs takes precedence in the sense that if subHubs==TRUE and trapErrors==FALSE, an error will be issued only if both

the principal component and the hubgene calculations have failed.

returnValidOnly

Boolean. Controls whether the returned data frames of module eigengenes contain columns corresponding only to modules whose eigengenes or hub genes

could be calculated correctly in every set (TRUE), or whether the data frame

should have columns for each of the input color labels (FALSE).

softPower The power used in soft-thresholding the adjacency matrix. Only used when the

> hubgene approximation is necessary because the principal component calculation failed. It must be non-negative. The default value should only be changed

if there is a clear indication that it leads to incorrect results.

Controls verbosity of printed progress messages. 0 means silent, up to (about) 5 verbose

the verbosity gradually increases.

indent A single non-negative integer controlling indentation of printed messages. 0

means no indentation, each unit above that adds two spaces.

Details

This function calls moduleEigengenes for each set in exprData.

Module eigengene is defined as the first principal component of the expression matrix of the corresponding module. The calculation may fail if the expression data has too many missing entries. 258 multiSetMEs

Handling of such errors is controlled by the arguments subHubs and trapErrors. If subHubs==TRUE, errors in principal component calculation will be trapped and a substitute calculation of hubgenes will be attempted. If this fails as well, behaviour depends on trapErrors: if TRUE, the offending module will be ignored and the return value will allow the user to remove the module from further analysis; if FALSE, the function will stop. If universalColors is given, any offending module will be removed from all sets (see validMEs in return value below).

From the user's point of view, setting trapErrors=FALSE ensures that if the function returns normally, there will be a valid eigengene (principal component or hubgene) for each of the input colors. If the user sets trapErrors=TRUE, all calculational (but not input) errors will be trapped, but the user should check the output (see below) to make sure all modules have a valid returned eigengene.

While the principal component calculation can fail even on relatively sound data (it does not take all that many "well-placed" NA to torpedo the calculation), it takes many more irregularities in the data for the hubgene calculation to fail. In fact such a failure signals there likely is something seriously wrong with the data.

Value

A vector of lists similar in spirit to the input exprData. For each set there is a list with the following components:

data Module eigengenes in a data frame, with each column corresponding to one

eigengene. The columns are named by the corresponding color with an "ME" prepended, e.g., MEturquoise etc. Note that, when trapErrors == TRUE and returnValidOnly==FALSE, this data frame also contains entries corresponding to removed modules, if any. (validMEs below indicates which eigengenes are valid and allOK whether all module eigengens were successfully calculated.)

averageExpr If align == "along average", a dataframe containing average normalized ex-

pression in each module. The columns are named by the corresponding color

with an "AE" prepended, e.g., AEturquoise etc.

varExplained A dataframe in which each column corresponds to a module, with the com-

ponent varExplained[PC, module] giving the variance of module module explained by the principal component no. PC. This is only accurate if all principal components have been computed (input nPC = NULL). At most 5 principal com-

ponents are recorded in this dataframe.

nPC A copy of the input nPC.

validMEs A boolean vector. Each component (corresponding to the columns in data) is

TRUE if the corresponding eigengene is valid, and FALSE if it is invalid. Valid eigengenes include both principal components and their hubgene approximations. When returnValidOnly==FALSE, by definition all returned eigengenes

are valid and the entries of validMEs are all TRUE.

validColors A copy of the input colors (universalColors if set, otherwise colors[, set])

with entries corresponding to invalid modules set to grey if given, otherwise 0

if the appropriate input colors are numeric and "grey" otherwise.

allok Boolean flag signalling whether all eigengenes have been calculated correctly,

either as principal components or as the hubgene approximation. If universalColors

is set, this flag signals whether all eigengenes are valid in all sets.

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allPC	Boolean flag signalling whether all returned eigengenes are principal components. This flag (as well as the subsequent ones) is set independently for each set.
isPC	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding eigengene is the first principal component and FALSE if it is the hubgene approximation or is invalid.
isHub	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding eigengene is the hubgene approximation and FALSE if it is the first principal component or is invalid.
validAEs	Boolean vector. Each component (corresponding to the columns in eigengenes) is TRUE if the corresponding module average expression is valid.
allAEOK	Boolean flag signalling whether all returned module average expressions contain valid data. Note that returnValidOnly==TRUE does not imply allAEOK==TRUE: some invalid average expressions may be returned if their corresponding eigengenes have been calculated correctly.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

See Also

 ${\tt module Eigengenes}$

multiUnion	Union and intersection of multiple sets	

Description

Union and intersection of multiple sets. These function generalize the standard functions union and intersect.

Usage

```
multiUnion(setList)
multiIntersect(setList)
```

Arguments

setList A list containing the sets to be performed upon.

Value

The union or intersection of the given sets.

Author(s)

Peter Langfelder

See Also

The "standard" functions union and intersect.

mutualInfoAdjacency

Calculate weighted adjacency matrices based on mutual information

Description

The function calculates different types of weighted adjacency matrices based on the mutual information between vectors (corresponding to the columns of the input data frame datE). The mutual information between pairs of vectors is divided by an upper bound so that the resulting normalized measure lies between 0 and 1.

Usage

```
mutualInfoAdjacency(
   datE,
   discretizeColumns = TRUE,
   entropyEstimationMethod = "MM",
   numberBins = NULL)
```

Arguments

datE

datE is a data frame or matrix whose columns correspond to variables and whose rows correspond to measurements. For example, the columns may correspond to genes while the rows correspond to microarrays. The number of nodes in the mutual information network equals the number of columns of datE.

discretizeColumns

is a logical variable. If it is set to TRUE then the columns of datE will be discretized into a user-defined number of bins (see numberBins).

entropyEstimationMethod

takes a text string for specifying the entropy and mutual information estimation method. If entropyEstimationMethod="MM" then the Miller-Madow asymptotic bias corrected empirical estimator is used. If entropyEstimationMethod="ML" the maximum likelihood estimator (also known as plug-in or empirical estimator) is used. If entropyEstimationMethod="shrink", the shrinkage estimator of a Dirichlet probability distribution is used. If entropyEstimationMethod="SG", the Schurmann-Grassberger estimator of the entropy of a Dirichlet probability distribution is used.

numberBins

is an integer larger than 0 which specifies how many bins are used for the discretization step. This argument is only relevant if discretizeColumns has been set to TRUE. By default numberBins is set to sqrt(m) where m is the number of samples, i.e. the number of rows of datE. Thus the default is numberBins=sqrt(nrow(datE)).

Details

The function inputs a data frame datE and outputs a list whose components correspond to different weighted network adjacency measures defined between the columns of datE. Make sure to install the following R packages entropy, minet, infotheo since the function mutualInfoAdjacency makes use of the entropy function from the R package entropy (Hausser and Strimmer 2008) and functions from the minet and infotheo package (Meyer et al 2008). A weighted network adjacency matrix is a symmetric matrix whose entries take on values between 0 and 1. Each weighted adjacency matrix contains scaled versions of the mutual information between the columns of the input data frame datE. We assume that datE contains numeric values which will be discretized unless the user chooses the option discretizeColumns=FALSE. The raw (unscaled) mutual information and entropy measures have units "nat", i.e. natural logarithms are used in their definition (base e=2.71..). Several mutual information estimation methods have been proposed in the literature (reviewed in Hausser and Strimmer 2008, Meyer et al 2008). While mutual information networks allows one to detect non-linear relationships between the columns of datE, they may overfit the data if relatively few observations are available. Thus, if the number of rows of datE is smaller than say 200, it may be better to fit a correlation using the function adjacency.

Value

The function outputs a list with the following components:

Entropy

is a vector whose components report entropy estimates of each column of datE. The natural logarithm (base e) is used in the definition. Using the notation from the Wikipedia entry (http://en.wikipedia.org/wiki/Mutual_information), this vector contains the values Hx where x corresponds to a column in datE.

MutualInformation

is a symmetric matrix whose entries contain the pairwise mutual information measures between the columns of datE. The diagonal of the matrix MutualInformation equals Entropy. In general, the entries of this matrix can be larger than 1, i.e. this is not an adjacency matrix. Using the notation from the Wikipedia entry, this matrix contains the mutual information estimates I(X;Y)

AdjacencySymmetricUncertainty

is a weighted adjacency matrix whose entries are based on the mutual information. Using the notation from the Wikipedia entry, this matrix contains the mutual information estimates AdjacencySymmetricUncertainty=2*I(X;Y)/(H(X)+H(Y)). Since I(X;X)=H(X), the diagonal elements of AdjacencySymmetricUncertainty equal 1. In general the entries of this symmetric matrix AdjacencySymmetricUncertainty lie between 0 and 1.

AdjacencyUniversalVersion1

is a weighted adjacency matrix that is a simple function of the AdjacencySymmetricUncertainty. Specifically, AdjacencyUniversalVersion1= AdjacencySymmetricUncertainty/(2-AdjacencySymmetricUncertainty). Note that f(x)=x/(2-x) is a monotonically increasing function on the unit interval [0,1] whose values lie between 0 and 1. The reason why we call it the universal adjacency is that dissUA=1-AdjacencyUniversalVersion1 turns out to be a universal distance function, i.e. it satisfies the properties of a distance (including the triangle inequality) and it takes on a small value if any other distance measure takes on a small value (Kraskov et al 2003).

AdjacencyUniversalVersion2

is a weighted adjacency matrix for which dissUAversion2=1-AdjacencyUniversalVersion2 is also a universal distance measure. Using the notation from Wikipedia, the entries of the symmetric matrix AdjacencyUniversalVersion2 are defined as follows AdjacencyUniversalVersion2= $I(X;Y)/\max(H(X),H(Y))$.

Author(s)

Steve Horvath, Lin Song, Peter Langfelder

References

Hausser J, Strimmer K (2008) Entropy inference and the James-Stein estimator, with application to nonlinear gene association networks. See http://arxiv.org/abs/0811.3579

Patrick E. Meyer, Frederic Lafitte, and Gianluca Bontempi. minet: A R/Bioconductor Package for Inferring Large Transcriptional Networks Using Mutual Information. BMC Bioinformatics, Vol 9, 2008

Kraskov A, Stoegbauer H, Andrzejak RG, Grassberger P (2003) Hierarchical Clustering Based on Mutual Information. ArXiv q-bio/0311039

See Also

adjacency

Examples

```
# Load requisite packages. These packages are considered "optional",
# so WGCNA does not load them automatically.
if (require(infotheo, quietly = TRUE) &&
    require(minet, quietly = TRUE) &&
    require(entropy, quietly = TRUE))
{
 # Example can be executed.
 #Simulate a data frame datE which contains 5 columns and 50 observations
 m = 50
 x1=rnorm(m)
 r=.5; x2=r*x1+sqrt(1-r^2)*rnorm(m)
 r=.3; x3=r*(x1-.5)^2+sqrt(1-r^2)*rnorm(m)
 x4=rnorm(m)
 r=.3; x5=r*x4+sqrt(1-r^2)*rnorm(m)
 datE=data.frame(x1,x2,x3,x4,x5)
 #calculate entropy, mutual information matrix and weighted adjacency
 # matrices based on mutual information.
 MIadj=mutualInfoAdjacency(datE=datE)
 printFlush(paste("Please install packages infotheo, minet and entropy",
                   "before running this example."));
```

nearestCentroidPredictor

Nearest centroid predictor

Description

Nearest centroid predictor for binary (i.e., two-outcome) data. Implements a whole host of options and improvements such as accounting for within-class heterogeneity using sample networks, various ways of feature selection and weighing etc.

Usage

```
nearestCentroidPredictor(
    # Input training and test data
    xtest = NULL,
    # Feature weights and selection criteria
    featureSignificance = NULL,
    assocFnc = "cor", assocOptions = "use = 'p'",
    assocCut.hi = NULL, assocCut.lo = NULL,
    nFeatures.hi = 10, nFeatures.lo = 10,
    weighFeaturesByAssociation = 0,
    scaleFeatureMean = TRUE, scaleFeatureVar = TRUE,
    # Predictor options
    centroidMethod = c("mean", "eigensample"),
    simFnc = "cor", simOptions = "use = 'p'",
    useQuantile = NULL,
    sampleWeights = NULL,
    weighSimByPrediction = 0,
    # What should be returned
    CVfold = 0, returnFactor = FALSE,
    # General options
    randomSeed = 12345,
    verbose = 2, indent = 0)
```

Arguments

- x Training features (predictive variables). Each column corresponds to a feature and each row to an observation.
- y The response variable. Can be a single vector or a matrix with arbitrary many columns. Number of rows (observations) must equal to the number of rows (observations) in x.

xtest

Optional test set data. A matrix of the same number of columns (i.e., features) as x. If test set data are not given, only the prediction on training data will be returned.

featureSignificance

Optional vector of feature significance for the response variable. If given, it is used for feature selection (see details). Should preferably be signed, that is features can have high negative significance.

assocFnc

Character string specifying the association function. The association function should behave roughly as link{cor} in that it takes two arguments (a matrix and a vector) plus options and returns the vector of associations between the columns of the matrix and the vector. The associations may be signed (i.e., negative or positive).

assocOptions

Character string specifying options to the association function.

assocCut.hi

Association (or featureSignificance) threshold for including features in the predictor. Features with associtation higher than assocCut.hi will be included. If not given, the threshold method will not be used; instead, a fixed number of features will be included as specified by nFeatures.hi and nFeatures.lo.

assocCut.lo

Association (or featureSignificance) threshold for including features in the predictor. Features with associtation lower than assocCut.lo will be included. If not given, defaults to -assocCut.hi. If assocCut.hi is NULL, the threshold method will not be used; instead, a fixed number of features will be included as specified by nFeatures.hi and nFeatures.lo.

nFeatures.hi

Number of highest-associated features (or features with highest featureSignificance) to include in the predictor. Only used if assocCut.hi is NULL.

nFeatures.lo

Number of lowest-associated features (or features with highest featureSignificance) to include in the predictor. Only used if assocCut.hi is NULL.

weighFeaturesByAssociation

(Optional) power to downweigh features that are less associated with the response. See details.

scaleFeatureMean

Logical: should the training features be scaled to mean zero? Unless there are good reasons not to scale, the features should be scaled.

scaleFeatureVar

Logical: should the training features be scaled to unit variance? Again, unless there are good reasons not to scale, the features should be scaled.

centroidMethod One of "mean" and "eigensample", specifies how the centroid should be calculated. "mean" takes the mean across all samples (or all samples within a sample module, if sample networks are used), whereas "eigensample" calculates the first principal component of the feature matrix and uses that as the centroid.

simFnc

Character string giving the similarity function for measuring the similarity between test samples and centroids. This function should behave roughly like the function cor in that it takes two arguments (x, y) and calculates the pair-wise similarities between columns of x and y. For convenience, the value "dist" is treated specially: the Euclidean distance between the columns of x and y is calculated and its negative is returned (so that smallest distance corresponds to highest similarity). Since values of this function are only used for ranking centroids, its values are not restricted to be positive or within certain bounds.

simOptions Character string specifying the options to the similarity function.

troid. See details.

sampleWeights Optional specification of sample weights. Useful for example if one wants to

explore boosting.

weighSimByPrediction

(Optional) power to downweigh features that are not well predicted between

training and test sets. See details.

CVfold Non-negative integer specifying cross-validation. Zero means no cross-validation

will be performed. values above zero specify the number of samples to be con-

sidered test data for each step of cross-validation.

returnFactor Logical: should a factor be returned?

randomSeed Integere specifying the seed for the random number generator. If NULL, the seed

will not be set. See set. seed.

verbose Integer controling how verbose the diagnostic messages should be. Zero means

silent.

indent Indentation for the diagnostic messages. Zero means no indentation, each unit

adds two spaces.

Details

Nearest centroid predictor works by forming a representative profile (centroid) across features for each class from the training data, then assigning each test sample to the class of the nearest representative profile. The representative profile can be formed either as mean or as athe first principal component ("eigensample"; this choice is governed by the option centroidMethod).

When the number of features is large and only a small fraction is likely to be associated with the outcome, feature selection can be used to restrict the features that actually enter the centroid. Feature selection can be based either on their association with the outcome calculated from the training data using assocFnc, or on user-supplied feature significance (e.g., derived from literature, argument featureSignificance). In either case, features can be selected by high and low association tresholds or by taking a fixed number of highest- and lowest-associated features.

As an alternative to centroids, the predictor can also assign test samples based on a given quantile of the distances from the training samples in each class (argument useQuantile). This may be advantageous if the samples in each class form irregular clusters. Note that setting useQuantile=0 (i.e., using minimum distance in each class) essentially gives a nearest neighbor predictor: each test sample will be assigned to the class of its nearest training neighbor.

If features exhibit non-trivial correlations among themselves (such as, for example, in gene expression data), one can attempt to down-weigh features that do not exhibit the same correlation in the test set. This is done by using essentially the same predictor to predict _features_ from all other features in the test data (using the training data to train the feature predictor). Because test features are known, the prediction accuracy can be evaluated. If a feature is predicted badly (meaning the error in the test set is much larger than the error in the cross-validation prediction in training data), it may mean that its quality in the training or test data is low (for example, due to excessive noise or outliers). Such features can be downweighed using the argument weighByPrediction. The extra factor is min(1, (root mean square prediction error in test set)/(root mean square cross-validation prediction error in the training data)^weighByPrediction), that is it is never bigger than 1.

Unless the features' mean and variance can be ascribed clear meaning, the (training) features should be scaled to mean 0 and variance 1 before the centroids are formed.

The function implements a basic option for removal of spurious effects in the training and test data, by removng a fixed number of leading principal components from the features. This sometimes leads to better prediction accuracy but should be used with caution.

If samples within each class are heterogenous, a single centroid may not represent each class well. This function can deal with within-class heterogeneity by clustering samples (separately in each class), then using a one representative (mean, eigensample) or quantile for each cluster in each class to assign test samples. Various similarity measures, specified by adjFnc, can be used to construct the sample network adjacency. Similarly, the user can specify a clustering function using clusteringFnc. The requirements on the clustering function are described in a separate section below.

Value

A list with the following components:

predicted The back-substitution prediction in the training set.

predictedTest Prediction in the test set.

featureSignificance

A vector of feature significance calculated by assocFnc or a copy of the input featureSignificance if the latter is non-NULL.

selectedFeatures

A vector giving the indices of the features that were selected for the predictor.

centroidProfile

The representative profiles of each class (or cluster). Only returned in useQuntile is NULL.

testSample2centroidSimilarities

A matrix of calculated similarities between the test samples and class/cluster centroids.

featureValidationWeights

A vector of validation weights (see Details) for the selected features. If weighFeaturesByValidation is 0, a unit vector is used and returned.

CVpredicted

Cross-validation prediction on the training data. Present only if CVfold is non-zero.

sampleClusterLabels

A list with two components (one per class). Each component is a vector of sample cluster labels for samples in the class.

Author(s)

Peter Langfelder

See Also

votingLinearPredictor

```
nearestNeighborConnectivity
```

Connectivity to a constant number of nearest neighbors

Description

Given expression data and basic network parameters, the function calculates connectivity of each gene to a given number of nearest neighbors.

Usage

Arguments

datExpr	a data frame containing expression data, with rows corresponding to samples and columns to genes. Missing values are allowed and will be ignored.
nNeighbors	number of nearest neighbors to use.
power	soft thresholding power for network construction. Should be a number greater than $1. $
type	a character string encoding network type. Recognized values are (unique abbreviations of) "unsigned", "signed", and "signed hybrid".
corFnc	character string containing the name of the function to calculate correlation. Suggested functions include "cor" and "bicor".
corOptions	further argument to the correlation function.
blockSize	correlation calculations will be split into square blocks of this size, to prevent running out of memory for large gene sets.
sampleLinks	logical: should network connections be sampled (TRUE) or should all connections be used systematically (FALSE)?
nLinks	number of links to be sampled. Should be set such that $nLinks * nNeighbors$ be several times larger than the number of genes.
setSeed	seed to be used for sampling, for repeatability. If a seed already exists, it is saved before the sampling starts and restored upon exit.
verbose	integer controlling the level of verbosity. 0 means silent.
indent	integer controlling indentation of output. Each unit above 0 adds two spaces.

Details

Connectivity of gene i is the sum of adjacency strengths between gene i and other genes; in this case we take the nNeighbors nodes with the highest connection strength to gene i. The adjacency strengths are calculated by correlating the given expression data using the function supplied in corFNC and transforming them into adjacency according to the given network type and power.

Value

A vector with one component for each gene containing the nearest neighbor connectivity.

Author(s)

Peter Langfelder

See Also

```
adjacency, softConnectivity
```

nearestNeighborConnectivityMS

Connectivity to a constant number of nearest neighbors across multiple data sets

Description

Given expression data from several sets and basic network parameters, the function calculates connectivity of each gene to a given number of nearest neighbors in each set.

Usage

Arguments

multiExpr expression data in multi-set format. A vector of lists, one list per set. In each list

there must be a component named data whose content is a matrix or dataframe or array of dimension 2 containing the expression data. Rows correspond to

samples and columns to genes (probes).

nNeighbors number of nearest neighbors to use.

power soft thresholding power for network construction. Should be a number greater

than 1.

type a character string encoding network type. Recognized values are (unique abbre-

viations of) "unsigned", "signed", and "signed hybrid".

corFnc	character string containing the name of the function to calculate correlation. Suggested functions include "cor" and "bicor".
corOptions	further argument to the correlation function.
blockSize	correlation calculations will be split into square blocks of this size, to prevent running out of memory for large gene sets.
sampleLinks	logical: should network connections be sampled (TRUE) or should all connections be used systematically (FALSE)?
nLinks	number of links to be sampled. Should be set such that nLinks \star nNeighbors be several times larger than the number of genes.
setSeed	seed to be used for sampling, for repeatability. If a seed already exists, it is saved before the sampling starts and restored after.
verbose	integer controlling the level of verbosity. 0 means silent.
indent	integer controlling indentation of output. Each unit above 0 adds two spaces.

Details

Connectivity of gene i is the sum of adjacency strengths between gene i and other genes; in this case we take the nNeighbors nodes with the highest connection strength to gene i. The adjacency strengths are calculated by correlating the given expression data using the function supplied in corFNC and transforming them into adjacency according to the given network type and power.

Value

A matrix in which columns correspond to sets and rows to genes; each entry contains the nearest neighbor connectivity of the corresponding gene.

Author(s)

Peter Langfelder

See Also

 ${\tt adjacency}, {\tt softConnectivity}, {\tt nearestNeighborConnectivity}$

networkConcepts Calculations of network concepts
--

Description

This functions calculates various network concepts (topological properties, network indices) of a network calculated from expression data. See details for a detailed description.

Usage

```
networkConcepts(datExpr, power = 1, trait = NULL, networkType = "unsigned")
```

Arguments

datExpr a data frame containg the expression data, with rows corresponding to samples

and columns to genes (nodes).

power soft thresholding power.

trait optional specification of a sample trait. A vector of length equal the number of

samples in datExpr.

networkType network type. Recognized values are (unique abbreviations of) "unsigned",

"signed", and "signed hybrid".

Details

This function computes various network concepts (also known as network statistics, topological properties, or network indices) for a weighted correlation network. The nodes of the weighted correlation network will be constructed between the columns (interpreted as nodes) of the input datExpr. If the option networkType="unsigned" then the adjacency between nodes i and j is defined as A[i,j]=abs(cor(datExpr[,i],datExpr[,j]))^power. In the following, we use the term gene and node interchangeably since these methods were originally developed for gene networks. The function computes the following 4 types of network concepts (introduced in Horvath and Dong 2008):

Type I: fundamental network concepts are defined as a function of the off-diagonal elements of an adjacency matrix A and/or a node significance measure GS. These network concepts can be defined for any network (not just correlation networks). The adjacency matrix of an unsigned weighted correlation network is given by A=abs(cor(datExpr,use="p"))^power and the trait based gene significance measure is given by GS= abs(cor(datExpr,trait, use="p"))^power where datExpr, trait, power are input parameters.

Type II: conformity-based network concepts are functions of the off-diagonal elements of the conformity based adjacency matrix A. CF=CF*t(CF) and/or the node significance measure. These network concepts are defined for any network for which a conformity vector can be defined. Details: For any adjacency matrix A, the conformity vector CF is calculated by requiring that A[i,j] is approximately equal to CF[i]*CF[j]. Using the conformity one can define the matrix A. CF=CF*t(CF) which is the outer product of the conformity vector with itself. In general, A. CF is not an adjacency matrix since its diagonal elements are different from 1. If the off-diagonal elements of A. CF are similar to those of A according to the Frobenius matrix norm, then A is approximately factorizable. To measure the factorizability of a network, one can calculate the Factorizability, which is a number between 0 and 1 (Dong and Horvath 2007). The conformity is defined using a monotonic, iterative algorithm that maximizes the factorizability measure.

Type III: approximate conformity based network concepts are functions of all elements of the conformity based adjacency matrix A.CF (including the diagonal) and/or the node significance measure GS. These network concepts are very useful for deriving relationships between network concepts in networks that are approximately factorizable.

Type IV: eigengene-based (also known as eigennode-based) network concepts are functions of the eigengene-based adjacency matrix A.E=ConformityE*t(ConformityE) (diagonal included) and/or the corresponding eigengene-based gene significance measure GSE. These network concepts can only be defined for correlation networks. Details: The columns (nodes) of datExpr can be summarized with the first principal component, which is referred to as Eigengene in coexpression network analysis. In general correlation networks, it is called eigennode. The eigengene-based conformity

ConformityE[i] is defined as abs(cor(datE[,i], Eigengene))^power where the power corresponds to the power used for defining the weighted adjacency matrix A. The eigengene-based conformity can also be used to define an eigengene-based adjacency matrix A. E=ConformityE*t(ConformityE). The eigengene based factorizability EF(datE) is a number between 0 and 1 that measures how well A.E approximates A when the power parameter equals 1. EF(datE) is defined with respect to the singular values of datExpr. For a trait based node significance measure GS=abs(cor(datE,trait))^power, one can also define an eigengene-based node significance measure GSE[i]=ConformityE[i]*EigengeneSignificance where the eigengene significance abs(cor(Eigengene,trait))^power is defined as power of the absolute value of the correlation between eigengene and trait. Eigengene-based network concepts are very useful for providing a geometric interpretation of network concepts and for deriving relationships between network concepts. For example, the hub gene significance measure and its eigengene-based analog have been used to characterize networks where highly connected hub genes are important with regard to a trait based gene significance measure (Horvath and Dong 2008).

Value

A list with the following components:

Summary a data frame whose rows report network concepts that only depend on the adja-

cency matrix. Density (mean adjacency), Centralization, Heterogeneity (coefficient of variation of the connectivity), Mean ClusterCoef, Mean Connectivity. The columns of the data frame report the 4 types of network concepts mentioned in the description: Fundamental concepts, eigengene-based concepts, conformity-based concepts, and approximate conformity-based concepts.

conformity-based concepts, and approximate conformity-based concepts.

Size reports the network size, i.e. the number of nodes, which equals the number of

columns of the input data frame datExpr.

Factorizability

a number between 0 and 1. The closer it is to 1, the better the off-diagonal elements of the conformity based network A.CF approximate those of A (according

to the Frobenius norm).

Eigengene the first principal component of the standardized columns of datExpr. The num-

ber of components of this vector equals the number of rows of datExpr.

VarExplained the proportion of variance explained by the first principal component (the Eigengene).

It is numerically different from the eigengene based factorizability. While VarExplained

is based on the squares of the singular values of datExpr, the eigengene-based

factorizability is based on fourth powers of the singular values.

Conformity numerical vector giving the conformity. The number of components of the con-

formity vector equals the number of columns in datExpr. The conformity is often highly correlated with the vector of node connectivities. The conformity is computed using an iterative algorithm for maximizing the factorizability measure. The algorithm and related network concepts are described in Dong and

Horvath 2007.

ClusterCoef a numerical vector that reports the cluster coefficient for each node. This funda-

mental network concept measures the cliquishness of each node.

Connectivity a numerical vector that reports the connectivity (also known as degree) of each

node. This fundamental network concept is also known as whole network con-

nectivity. One can also define the scaled connectivity K=Connectivity/max(Connectivity)

which is used for computing the hub gene significance.

MAR a numerical vector that reports the maximum adjacency ratio for each node.

MAR[i] equals 1 if all non-zero adjacencies between node i and the remaining network nodes equal 1. This fundamental network concept is always 1 for nodes of an unweighted network. This is a useful measure for weighted networks since it allows one to determine whether a node has high connectivity because of many weak connections (small MAR) or because of strong (but few) connections (high

MAR), see Horvath and Dong 2008.

ConformityE a numerical vector that reports the eigengene based (aka eigenenode based) con-

formity for the correlation network. The number of components equals the num-

ber of columns of datExpr.

a numerical vector that encodes the node (gene) significance. The i-th compo-

nent equals the node significance of the i-th column of datExpr if a sample trait was supplied to the function (input trait). GS[i]=abs(cor(datE[,i], trait, date))

use="p"))^power

GSE a numerical vector that reports the eigengene based gene significance measure.

Its i-th component is given by GSE[i]=ConformityE[i]*EigengeneSignificance where the eigengene significance abs(cor(Eigengene,trait))^power is defined as power of the absolute value of the correlation between eigengene and

trait.

Significance a data frame whose rows report network concepts that also depend on the trait

based node significance measure. The rows correspond to network concepts and the columns correspond to the type of network concept (fundamental versus eigengene based). The first row of the data frame reports the network significance. The fundamental version of this network concepts is the average gene significance=mean(GS). The eigengene based analog of this concept is defined as mean(GSE). The second row reports the hub gene significance which is defined as slope of the intercept only regression model that regresses the gene significance on the scaled network connectivity K. The third row reports the eigengene significance abs(cor(Eigengene, trait))^power. More details can be found

in Horvath and Dong (2008).

Author(s)

Jun Dong, Steve Horvath, Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

See Also

conformityBasedNetworkConcepts for approximate conformity-based network concepts

networkScreening 273

fundamentalNetworkConcepts for calculation of fundamental network concepts only.

Description

This function blends standard and network approaches to selecting genes (or variables in general) highly related to a given trait.

Usage

Arguments

	У	clinical trait given as a numeric vector (one value per sample)	
	datME	data frame of module eigengenes	
	datExpr	data frame of expression data	
	corFnc	character string specifying the function to be used to calculate co-expression similarity. Defaults to Pearson correlation. Any function returning values between -1 and 1 can be used.	
	corOptions	character string specifying additional arguments to be passed to the function given by corFnc. Use "use = 'p', method = 'spearman'" to obtain Spearman correlation.	
	oddPower	odd integer used as a power to raise module memberships and significances	
	blockSize	block size to use for calculations with large data sets	
minimumSampleSize		ze	
		minimum acceptable number of samples. Defaults to the default minimum number of samples used throughout the WGCNA package, currently 4.	
	addMEy	logical: should the trait be used as an additional "module eigengene"?	
	removeDiag	logical: remove the diagonal?	

Details

weightESy

getQValues

This function should be considered experimental. It takes into account both the "standard" and the network measures of gene importance for the trait.

logical: should q-values be calculated?

weight to use for the trait as an additional eigengene; should be between 0 and 1

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Value

datout = data.frame(p.Weighted, q.Weighted, Cor.Weighted, Z.Weighted, p.Standard, q.Standard, Cor.Standard, Z.Standard) Data frame reporting the following quantities for each given gene:

p.Weighted weighted p-value of association with the trait q.Weighted q-value (local FDR) calculated from p.Weighted

cor. Weighted correlation of trait with gene expression weighted by a network term

Z. Weighted Fisher Z score of the weighted correlation

p. Standard Student p-value of association of the gene with the trait

q. Standard q-value (local FDR) calculated from p. Standard

cor. Standard correlation of gene with the trait

Z. Standard Fisher Z score of the standard correlation

Author(s)

Steve Horvath

networkScreeningGS

Network gene screening with an external gene significance measure

Description

This function blends standard and network approaches to selecting genes (or variables in general) with high gene significance

Usage

```
networkScreeningGS(
  datExpr,
  datME,
  GS,
  oddPower = 3,
  blockSize = 1000,
  minimumSampleSize = ..minNSamples,
  addGS = TRUE)
```

Arguments

datExpr data frame of expression data
datME data frame of module eigengenes
numeric vector of gene significances

oddPower odd integer used as a power to raise module memberships and significances

blockSize block size to use for calculations with large data sets

minimumSampleSize

minimum acceptable number of samples. Defaults to the default minimum num-

ber of samples used throughout the WGCNA package, currently 4.

addGS logical: should gene significances be added to the screening statistics?

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Details

This function should be considered experimental. It takes into account both the "standard" and the network measures of gene importance for the trait.

Value

GS. Weighted weighted gene significance

GS copy of the input gene significances (only if addGS=TRUE)

Author(s)

Steve Horvath

See Also

networkScreening, automaticNetworkScreeningGS

newBlockInformation

Create a list holding information about dividing data into blocks

Description

This function creates a list storing information about dividing data into blocks, as well as about possibly excluding genes or samples with excessive numbers of missing data.

Usage

newBlockInformation(blocks, goodSamplesAndGenes)

Arguments

blocks A vector giving block labels. It is assumed to be a numeric vector with block

labels consecutive integers starting at 1.

goodSamplesAndGenes

A list returned by goodSamplesGenes or goodSamplesGenesMS.

Value

A list with class attribute set to BlockInformation, with the following componens:

blocks A copy of the input blocks.

blockGenes A list with one component per block, giving the indices of elements in block

whose value is the same.

goodSamplesAndGenes

A copy of input goodSamplesAndGenes.

nGGenes Number of 'good' genes in goodSamplesAndGenes.

gBlocks The input blocks restricted to 'good' genes in goodSamplesAndGenes.

276 newBlockwiseData

Author(s)

Peter Langfelder

See Also

goodSamplesGenesMS.

newBlockwiseData

Create, merge and expand BlockwiseData objects

Description

These functions create, merge and expand BlockwiseData objects for holding in-memory or disk-backed blockwise data. Blockwise here means that the data is too large to be loaded or processed in one piece and is therefore split into blocks that can be handled one by one in a divide-and-conquer manner.

Usage

```
newBlockwiseData(
   data,
   external = FALSE,
   fileNames = NULL,
   doSave = external,
   recordAttributes = TRUE,
   metaData = list())
mergeBlockwiseData(...)
addBlockToBlockwiseData(
  bwData,
  blockData,
   external = bwData$external,
   blockFile = NULL,
   doSave = external,
   recordAttributes = !is.null(bwData$attributes),
   metaData = NULL)
```

Arguments

data A list in which each component carries the data of a single block.

external Logical: should the data be disk-backed (TRUE) or in-memory (FALSE)?

fileNames When external is TRUE, this argument must be a character vector of the same

length as data, giving the file names for the data to be saved to, or where the

data is already located.

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doSave Logical: should data be saved? If this is FALSE, it is the user's responsibility to

ensure the files supplied in fileNames already exist and contain the expected $\ensuremath{\mathsf{I}}$

data.

recordAttributes

Logical: should attributes of the given data be recorded within the object?

metaData A list giving any additional meta-data for data that should be attached to the

object.

bwData An existing BlockwiseData object.

blockData A vector, matrix or array carrying the data of a single block.

blockFile File name where data contained in blockData should be saved.

... One or more objects of class BlockwiseData.

Details

Several functions in this package use the concept of blockwise, or "divide-and-conquer", analysis. The BlockwiseData class is meant to hold the blockwise data, or all necessary information about blockwise data that is saved in disk files.

The data can be stored in disk files (one file per block) or in-memory. In memory storage is provided so that same code can be used for both smaller (single-block) data where disk storage could slow down operations as well as larger data sets where disk storage and block by block analysis are necessary.

Value

All three functions return a list with the class set to "BlockwiseData", containing the following components:

external Copy of the input argument external

data If external is TRUE, an empty list, otherwise a copy of the input data.

fileNames Copy of the input argument fileNames.

lengths A vector of lengths (results of length) of elements of data.

attributes If input recordAttributes is TRUE, a list with one component per block (com-

ponent of data); each component is in turn a list of attributes of that component

of data.

metaData A copy of the input metaData.

Warning

The definition of BlockwiseData should be considered experimental and may change in the future.

Author(s)

Peter Langfelder

See Also

Other functions on BlockwiseData:

```
BD. getData for retrieving data
```

- BD. actualFileNames for retrieving file names of files containing data;
- BD. nBlocks for retrieving the number of blocks;
- BD.blockLengths for retrieving block lengths;
- BD.getMetaData for retrieving metadata;
- BD. checkAndDeleteFiles for deleting files of an unneeded object.

newConsensusOptions

Create a list holding consensus calculation options.

Description

This function creates a list of class ConsensusOptions that holds options for consensus calculations. This list holds options for a single-level analysis.

Usage

```
newConsensusOptions(
    calibration = c("full quantile", "single quantile", "none"),

# Simple quantile scaling options
    calibrationQuantile = 0.95,
    sampleForCalibration = TRUE,
    sampleForCalibrationFactor = 1000,

# Consensus definition
    consensusQuantile = 0,
    useMean = FALSE,
    setWeights = NULL,
    suppressNegativeResults = FALSE,
    # Name to prevent files clashes
    analysisName = "")
```

Arguments

```
calibration Calibration method. One of "full quantile", "single quantile", "none" (or a unique abbreviation of one of them).
```

calibrationQuantile

if calibration is "single quantile", input data to a consensus calculation will be scaled such that their calibrationQuantile quantiles will agree.

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sampleForCalibration

if TRUE, calibration quantiles will be determined from a sample of network similarities. Note that using all data can double the memory footprint of the function and the function may fail.

sampleForCalibrationFactor

Determines the number of samples for calibration: the number is 1/calibrationQuantile * sampleForCalibrationFactor. Should be set well above 1 to ensure accuracy of the sampled quantile.

consensusQuantile

Quantile at which consensus is to be defined. See details.

useMean Logical: should the consensus be calculated using (weighted) mean rather than

a quantile?

setWeights Optional specification of weights when useMean is TRUE.

suppressNegativeResults

Logical: should negative consensus results be replaced by 0? In a typical network connstruction, negative topological overlap values may results with TOMType

= "signed Nowick".

analysisName Optional character string naming the consensus analysis. Useful for identifying

partial consensus calculation in hierarchical consensus analysis.

Value

A list of type ConsensusOptions that holds copies of the input arguments.

Author(s)

Peter Langfelder

newConsensusTree

Create a new consensus tree

Description

This function creates a new consensus tree, a class for representing "recipes" for hierarchical consensus calculations.

Usage

```
newConsensusTree(
   consensusOptions = newConsensusOptions(),
   inputs,
   analysisName = NULL)
```

Arguments

consensusOptions

An object of class ConsensusOptions, usually obtained by calling newConsensusOptions.

inputs A vector (or list) of inputs. Each component can be either a character string

giving a names of a data set, or another ConsensusTree object.

analysisName Optional specification of a name for this consensus analysis. While this has

no effect on the actual consensus calculation, some functions use this character

string to make certain file names unique.

Details

Consensus trees specify a "recipe" for the calculation of hierarchical consensus in hierarchicalConsensusCalculation and other functions.

Value

A list with class set to "ConsensusTree" with these components:

consensusOptions

A copy of the input consensusOptions.

inputs A copy of the input inputs.

analysisName A copy of the input analysisName.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusCalculation for hierarchical consensus calculation for which a ConsensusTree object specifies the recipe

newCorrelationOptions Creates a list of correlation options.

Description

Convenience function to create a re-usable list of correlation options.

Usage

```
newCorrelationOptions(
      corType = c("pearson", "bicor"),
      maxPOutliers = 0.05,
      quickCor = 0,
      pearsonFallback = "individual",
      cosineCorrelation = FALSE,
      nThreads = 0,
      corFnc = if (corType=="bicor") "bicor" else "cor",
      corOptions = c(
        list(use = 'p',
             cosine = cosineCorrelation,
             quick = quickCor,
             nThreads = nThreads),
        if (corType=="bicor")
           list(maxPOutliers = maxPOutliers,
                pearsonFallback = pearsonFallback) else NULL))
```

Arguments

corType

Character specifying the type of correlation function. Currently supported options are "pearson", "bicor".

maxPOutliers

Maximum proportion of outliers for biweight mid-correlation. See bicor.

quickCor

Real number between 0 and 1 that controls the handling of missing data in the calculation of correlations. See bicor.

pearsonFallback

Specifies whether the bicor calculation should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE).

cosineCorrelation

Logical: calculate cosine biweight midcorrelation? Cosine bicorrelation is similar to standard bicorrelation but the median subtraction is not performed.

nThreads

A non-negative integer specifying the number of parallel threads to be used by certain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads.

corFnc

Correlation function to be called in R code. Should correspoind to the value of corType above.

corOptions

A list of options to be supplied to the correlation function (in addition to appropriate arguments x and y).

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Value

A list containing a copy of the input arguments. The output has class CorrelationOptions.

Author(s)

Peter Langfelder

newNetworkOptions

Create a list of network construction arguments (options).

Description

This function creates a reusable list of network calculation arguments/options.

Usage

Arguments

```
correlationOptions
```

A list of correlation options. See newCorrelationOptions.

replaceMissingAdjacencies

Logical: should missing adjacencies be replaced by zero?

power Soft-thresholding power for network construction.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

checkPower Logicel: should the power be checked for sanity?

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TOMType One of "none", "unsigned", "signed Nowick", "unsigned 2", "signed

2" and "signed Nowick 2". If "none", adjacency will be used for clustering.

See TOMsimilarityFromExpr for details.

TOMDenom Character string specifying the TOM variant to be used. Recognized values

are "min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results but at this time should be considered

experimental.

suppressTOMForZeroAdjacencies

logical: for those components that have zero adjacency, should TOM be set to

zero as well?

suppressNegativeTOM

Logical: should the result be set to zero when negative? Negative TOM values

can occur when TOMType is "signed Nowick".

newNetworkOptions

useInternalMatrixAlgebra

logical: should internal implementation of matrix multiplication be used instead of R-provided BLAS? The internal implementation is slow and this option

should only be used if one suspects a bug in R-provided BLAS.

Value

A list of class NetworkOptions.

Author(s)

Peter Langfelder

See Also

newCorrelationOptions

normalizeLabels

Transform numerical labels into normal order.

Description

Transforms numerical labels into normal order, that is the largest group will be labeled 1, next largest 2 etc. Label 0 is optionally preserved.

Usage

normalizeLabels(labels, keepZero = TRUE)

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Arguments

labels Numerical labels.

keepZero If TRUE (the default), labels 0 are preserved.

Value

A vector of the same length as input, containing the normalized labels.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

nPresent

Number of present data entries.

Description

A simple sum of present entries in the argument.

Usage

nPresent(x)

Arguments

х

data in which to count number of present entries.

Value

A single number giving the number of present entries in x.

Author(s)

Steve Horvath

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nSets

Number of sets in a multi-set variable

Description

A convenience function that returns the number of sets in a multi-set variable.

Usage

```
nSets(multiData, ...)
```

Arguments

multiData vector of lists; in each list there must be a component named data whose content is a matrix or dataframe or array of dimension 2.... Other arguments to function checkSets.

Value

A single integer that equals the number of sets given in the input multiData.

Author(s)

Peter Langfelder

See Also

checkSets

numbers2colors

Color representation for a numeric variable

Description

The function creates a color represenation for the given numeric input.

Usage

```
numbers2colors(
    x,
    signed = NULL,
    centered = signed,
    lim = NULL,
    commonLim = FALSE,
    colors = if (signed) blueWhiteRed(100) else blueWhiteRed(100)[51:100],
    naColor = "grey")
```

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Arguments

x a vector or matrix of numbers. Missing values are allowed and will be assigned the color given in naColor. If a matrix, each column of the matrix is processed

separately and the return value will be a matrix of colors.

signed logical: should x be considered signed? If TRUE, the default setting is to use

to use a palette that starts with green for the most negative values, continues with white for values around zero and turns red for positive values. If FALSE, the default palette ranges from white for minimum values to red for maximum values. If not given, the behaviour is controlled by values in x: if there are both positive and negative values, signed will be considered TRUE, otherwise FALSE.

centered logical. If TRUE and signed==TRUE, numeric value zero will correspond to the

middle of the color palette. If FALSE or signed==FALSE, the middle of the color palette will correspond to the average of the minimum and maximum value. If neither signed nor centered are given, centered will follow signed (see

above).

1im optional specification of limits, that is numeric values that should correspond to

the first and last entry of colors.

commonLim logical: should limits be calculated separately for each column of x, or should

the limits be the same for all columns? Only applies if lim is NULL.

colors color palette to represent the given numbers.

naColor color to represent missing values in x.

Details

Each column of x is processed individually, meaning that the color palette is adjusted individually for each column of x.

Value

A vector or matrix (of the same dimensions as x) of colors.

Author(s)

Peter Langfelder

See Also

labels2colors for color coding of ordinal labels.

order Branches Using Hub Genes

Optimize dendrogram using branch swaps and reflections.

Description

This function takes as input the hierarchical clustering tree as well as a subset of genes in the network (generally corresponding to branches in the tree), then returns a semi-optimally ordered tree. The idea is to maximize the correlations between adjacent branches in the dendrogram, in as much as that is possible by adjusting the arbitrary positionings of the branches by swapping and reflecting branches.

Usage

```
orderBranchesUsingHubGenes(
  hierTOM,
  datExpr = NULL, colorh = NULL,
  type = "signed", adj = NULL, iter = NULL,
  useReflections = FALSE, allowNonoptimalSwaps = FALSE)
```

Arguments

hierTOM	A hierarchical clustering object (or gene tree) that is used to plot the dendrogram. For example, the output object from the function hclust or fastcluster::hclust. Note that elements of hierTOM\$order MUST be named (for example, with the corresponding gene name).
datExpr	Gene expression data with rows as samples and columns as genes, or NULL if a pre-made adjacency is entered. Column names of datExpr must be a subset of gene names of hierTOM\$order.
colorh	The module assignments (color vectors) corresponding to the rows in $datExpr$, or NULL if a pre-made adjacency is entered.
type	What type of network is being entered. Common choices are "signed" (default) and "unsigned". With "signed" negative correlations count against, whereas with "unsigned" negative correlations are treated identically as positive correlations.
adj	Either NULL (default) or an adjacency (or any other square) matrix with rows and columns corresponding to a subset of the genes in hierTOM\$order. If entered, datExpr, colorh, and type are all ignored. Typically, this would be left blank but could include correlations between module eigengenes, with rows and columns renamed as genes in the corresponding modules, for example.
iter	The number of iterations to run the function in search of optimal branch ordering. The default is the square of the number of modules (or the quare of the number of genes in the adjacency matrix).
useReflections	If TRUE, both reflections and branch swapping will be used to optimize dendrogram. If FALSE (default) only branch swapping will be used.

allowNonoptimalSwaps

If TRUE, there is chance (that decreases with each iteration) of swapping / reflecting branches whether or not the new correlation between expression of genes in adjacent branches is better or worse. The idea (which has not been sufficiently tested), is that this would prevent the function from getting stuck at a local maxima of correlation. If FALSE (default), the swapping / reflection of branches only occurs if it results in a higher correlation between adjacent branches.

Value

hierTOM A hierarchical clustering object with the hierTOM\$order variable properly ad-

justed, but all other variables identical as the heirTOM input.

changeLog A log of all of the changes that were made to the dendrogram, including what

change was made, on what iteration, and the Old and New scores based on correlation. These scores have arbitrary units, but higher is better.

Note

This function is very slow and is still in an *experimental* function. We have not had problems with ~10 modules across ~5000 genes, although theoretically it should work for many more genes and modules, depending upon the speed of the computer running R. Please address any problems or suggestions to jeremyinla@gmail.com.

Author(s)

Jeremy Miller

Examples

```
## Not run:
## Example: first simulate some data.
MEturquoise = sample(1:100,50)
           = c(MEturquoise[1:25], sample(1:100,25))
MEblue
MEbrown
            = sample(1:100,50)
MEyellow
            = sample(1:100,50)
MEgreen
            = c(MEyellow[1:30], sample(1:100,20))
MEred
          = c(MEbrown [1:20], sample(1:100,30))
       = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen, MEred)
       = simulateDatExpr(ME,400,c(0.16,0.12,0.11,0.10,0.10,0.10,0.1), signed=TRUE)
       = TOMsimilarityFromExpr(dat1$datExpr, networkType="signed")
colnames(TOM1) <- rownames(TOM1) <- colnames(dat1$datExpr)</pre>
tree1 = fastcluster::hclust(as.dist(1-TOM1),method="average")
colorh = labels2colors(dat1$allLabels)
plotDendroAndColors(tree1,colorh,dendroLabels=FALSE)
## Reassign modules using the selectBranch and chooseOneHubInEachModule functions
datExpr = dat1$datExpr
```

orderMEs 289

```
= chooseOneHubInEachModule(datExpr, colorh)
colorh2 = rep("grey", length(colorh))
colorh2 [selectBranch(tree1,hubs["blue"],hubs["turquoise"])] = "blue"
colorh2 [selectBranch(tree1,hubs["turquoise"],hubs["blue"])] = "turquoise"
colorh2 [selectBranch(tree1, hubs["green"], hubs["yellow"])] = "green"
colorh2 [selectBranch(tree1,hubs["yellow"],hubs["green"])] = "yellow"
                                                             = "red"
colorh2 [selectBranch(tree1, hubs["red"], hubs["brown"])]
colorh2 [selectBranch(tree1,hubs["brown"],hubs["red"])]
                                                             = "brown"
plotDendroAndColors(tree1,cbind(colorh,colorh2),c("Old","New"),dendroLabels=FALSE)
## Now swap and reflect some branches, then optimize the order of the branches
# and output pdf with resulting images
pdf("DENDROGRAM_PLOTS.pdf",width=10,height=5)
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Starting Dendrogram")
tree1 = swapTwoBranches(tree1,hubs["red"],hubs["turquoise"])
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Swap blue/turquoise and red/brown")
tree1 = reflectBranch(tree1,hubs["blue"],hubs["green"])
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Reflect turquoise/blue")
# (This function will take a few minutes)
out = orderBranchesUsingHubGenes(tree1,datExpr,colorh2,useReflections=TRUE,iter=100)
tree1 = out$geneTree
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Semi-optimal branch order")
out$changeLog
dev.off()
## End(Not run)
```

orderMEs

Put close eigenvectors next to each other

Description

Reorder given (eigen-)vectors such that similar ones (as measured by correlation) are next to each other.

Usage

290 orderMEs

Arguments

MEs	Module eigengenes in a multi-set format (see checkSets). A vector of lists, with each list corresponding to one dataset and the module eigengenes in the component data, that is MEs[[set]]\$data[sample, module] is the expression of the eigengene of module module in sample sample in dataset set. The number of samples can be different between the sets, but the modules must be the same.
greyLast	Normally the color grey is reserved for unassigned genes; hence the grey module is not a proper module and it is conventional to put it last. If this is not desired, set the parameter to FALSE.
greyName	Name of the grey module eigengene.
orderBy	Specifies the set by which the eigengenes are to be ordered (in all other sets as well). Defaults to the first set in useSets (or the first set, if useSets is not given).
order	Allows the user to specify a custom ordering.
useSets	Allows the user to specify for which sets the eigengene ordering is to be performed.
verbose	Controls verbostity of printed progress messages. 0 means silent, nonzero verbose.
indent	A single non-negative integer controling indentation of printed messages. 0 means no indentation, each unit above zero adds two spaces.

Details

Ordering module eigengenes is useful for plotting purposes. For this function the order can be specified explicitly, or a set can be given in which the correlations of the eigengenes will determine the order. For the latter, a hierarchical dendrogram is calculated and the order given by the dendrogram is used for the eigengenes in all other sets.

Value

A vector of lists of the same type as MEs containing the re-ordered eigengenes.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

See Also

moduleEigengenes, multiSetMEs, consensusOrderMEs

orderMEsByHierarchicalConsensus

Order module eigengenes by their hierarchical consensus similarity

Description

This function calculates a hiearchical consensus similarity of the input eigengenes, clusters the eigengenes according to the similarity and returns the input module eigengenes ordered by the order of resulting dendrogram.

Usage

```
orderMEsByHierarchicalConsensus(
    MEs,
    networkOptions,
    consensusTree,
    greyName = "ME0",
    calibrate = FALSE)
```

Arguments

MEs	Module eigengenes, or more generally, vectors, to be ordered, in a multiData format: A vector of lists, one per set. Each set must contain a component data that contains the module eigenegens or general vectors, with rows corresponding to samples and columns to genes or probes.
networkOptions	A single list of class NetworkOptions giving options for network calculation for all of the networks, or a multiData structure containing one such list for each input data set.
consensusTree	A list specifying the consensus calculation. See newConsensusTree for details.
greyName	Specifies the column name of eigengene of the "module" that contains unassigned genes. This eigengene (column) will be excluded from the clustering and will be put last in the order.
calibrate	Logical: should module eigengene similarities be calibrated? This setting overrides the calibration options in consensusTree.

Value

A multiData structure of the same format as the input MEs, with columns ordered by the calculated dendrogram.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusMEDissimilarity for calculating the consensus ME dissimilarity

292 overlapTable

|--|

Description

The function calculates overlap counts and Fisher exact test p-values for the given two sets of module assignments.

Usage

```
overlapTable(
   labels1, labels2,
   na.rm = TRUE, ignore = NULL,
   levels1 = NULL, levels2 = NULL,
   log.p = FALSE)
```

Arguments

labels1	a vector containing module labels.
labels2	a vector containing module labels to be compared to labels1.
na.rm	logical: should entries missing in either labels1 or labels2 be removed?
ignore	an optional vector giving label levels that are to be ignored.
levels1	optional vector giving levels for labels1. Defaults to sorted unique non-missing values in labels1 that are not present in ignore.
levels2	optional vector giving levels for labels2. Defaults to sorted unique non-missing values in labels2 that are not present in ignore.
log.p	logical: should (natural) logarithms of the p-values be returned instead of the p-values?

Value

A list with the following components:

countTable a matrix whose rows correspond to modules (unique labels) in labels1 and

whose columns correspond to modules (unique labels) in labels2, giving the

number of objects in the intersection of the two respective modules.

pTable a matrix whose rows correspond to modules (unique labels) in labels1 and

whose columns correspond to modules (unique labels) in labels2, giving Fisher's exact test significance p-values (or their logarithms) for the overlap of the two

respective modules.

Author(s)

Peter Langfelder

See Also

```
fisher.test, matchLabels
```

overlapTableUsingKME

Determines significant overlap between modules in two networks based on kME tables.

Description

Takes two sets of expression data (or kME tables) as input and returns a table listing the significant overlap between each module in each data set, as well as the actual genes in common for every module pair. Modules can be defined in several ways (generally involving kME) based on user input.

Usage

```
overlapTableUsingKME(
   dat1, dat2,
   colorh1, colorh2,
   MEs1 = NULL, MEs2 = NULL,
   name1 = "MM1", name2 = "MM2",
   cutoffMethod = "assigned", cutoff = 0.5,
   omitGrey = TRUE, datIsExpression = TRUE)
```

Arguments

dat1, dat2

Either expression data sets (with samples as rows and genes as columns) or module membership (kME) tables (with genes as rows and modules as columns). Function reads these inputs based on whether datIsExpression=TRUE or FALSE. ***Be sure that these inputs include relevant row and column names, or else the function will not work properly.***

colorh1, colorh2

Color vector (module assignments) corresponding to the genes from dat1/2. This vector must be the same length as the Gene dimension from dat1/2.

MEs1, MEs2

If entered (default=NULL), these are the module eigengenes that will be used to form the kME tables. Rows are samples and columns are module assignments. Note that if datIsExpression=FALSE, these inputs are ignored.

name1, name2

The names of the two data sets being compared. These names affect the output parameters.

cutoffMethod

This variable is used to determine how modules are defined in each data set. Must be one of four options: (1) "assigned" -> use the module assignments in colorh (default); (2) "kME" -> any gene with kME > cutoff is in the module; (3) "numGenes" -> the top cutoff number of genes based on kME is in the module; and (4) "pvalue" -> any gene with correlation pvalue < cutoff is in the module (this includes both positively and negatively-correlated genes).

cutoff For all cutoffMethods other than "assigned", this parameter is used as the de-

scribed cutoff value.

omitGrey If TRUE the grey modules (non-module genes) for both networks are not re-

turned.

datIsExpression

If TRUE (default), dat1/2 is assumed to be expression data. If FALSE, dat1/2 is assumed to be a table of kME values.

Value

PvaluesHypergeo

A table of p-values showing significance of module overlap based on the hypergeometric test. Note that these p-values are not corrected for multiple comparisons.

AllCommonGenes A character vector of all genes in common between the two data sets.

Genes<name1/2> A list of character vectors of all genes in each module in both data sets. All

genes in the MOD module in data set MM1 could be found using "<outputVari-

ableName>\$GenesMM1\$MM1_MOD"

OverlappingGenes

A list of character vectors of all genes for each between-set comparison from PvaluesHypergeo. All genes in MOD.A from MM1 that are also in MOD.B

from MM2 could be found using "<output VariableName>\$OverlappingGenes\$MM1_MOD.A_MM2_M

Author(s)

Jeremy Miller

See Also

overlapTable

Examples

pickHardThreshold 295

pickHardThreshold

Analysis of scale free topology for hard-thresholding.

Description

Analysis of scale free topology for multiple hard thresholds. The aim is to help the user pick an appropriate threshold for network construction.

Usage

```
pickHardThreshold(
  data,
  dataIsExpr,
  RsquaredCut = 0.85,
  cutVector = seq(0.1, 0.9, by = 0.05),
  moreNetworkConcepts = FALSE,
  removeFirst = FALSE, nBreaks = 10,
  corFnc = "cor", corOptions = "use = 'p'")

pickHardThreshold.fromSimilarity(
  similarity,
  RsquaredCut = 0.85,
  cutVector = seq(0.1, 0.9, by = 0.05),
  moreNetworkConcepts=FALSE,
  removeFirst = FALSE, nBreaks = 10)
```

Arguments

data	expression data in a matrix or data frame. Rows correspond to samples and columns to genes.
dataIsExpr	logical: should the data be interpreted as expression (or other numeric) data, or as a similarity matrix of network nodes?
similarity	similarity matrix: a symmetric matrix with entries between -1 and 1 and unit diagonal.

296 pickHardThreshold

RsquaredCut desired minimum scale free topology fitting index R^2 .

cutVector a vector of hard threshold cuts for which the scale free topology fit indices are

to be calculated.

moreNetworkConcepts

logical: should additional network concepts be calculated? If TRUE, the function will calculate how the network density, the network heterogeneity, and the network centralization depend on the power. For the definition of these additional

network concepts, see Horvath and Dong (2008). PloS Comp Biol.

removeFirst should the first bin be removed from the connectivity histogram?

nBreaks number of bins in connectivity histograms

corFnc a character string giving the correlation function to be used in adjacency calcu-

lation.

corOptions further options to the correlation function specified in corFnc.

Details

The function calculates unsigned networks by thresholding the correlation matrix using thresholds given in cutVector. For each power the scale free topology fit index is calculated and returned along with other information on connectivity.

Value

A list with the following components:

cutEstimate estimate of an appropriate hard-thresholding cut: the lowest cut for which the

scale free topology fit \mathbb{R}^2 exceeds RsquaredCut. If \mathbb{R}^2 is below RsquaredCut

for all cuts, NA is returned.

fitIndices a data frame containing the fit indices for scale free topology. The columns con-

tain the hard threshold, Student p-value for the correlation threshold, adjusted \mathbb{R}^2 for the linear fit, the linear coefficient, adjusted \mathbb{R}^2 for a more complicated fit models, mean connectivity, median connectivity and maximum connectivity. If input moreNetworkConcepts is TRUE, 3 additional columns containing network

density, centralization, and heterogeneity.

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

See Also

signumAdjacencyFunction

pickSoftThreshold 297

pickSoftThreshold

Analysis of scale free topology for soft-thresholding

Description

Analysis of scale free topology for multiple soft thresholding powers. The aim is to help the user pick an appropriate soft-thresholding power for network construction.

Usage

```
pickSoftThreshold(
  data,
  dataIsExpr = TRUE,
 weights = NULL,
 RsquaredCut = 0.85,
  powerVector = c(seq(1, 10, by = 1), seq(12, 20, by = 2)),
  removeFirst = FALSE, nBreaks = 10, blockSize = NULL,
  corFnc = cor, corOptions = list(use = 'p'),
  networkType = "unsigned",
  moreNetworkConcepts = FALSE,
  gcInterval = NULL,
  verbose = 0, indent = 0)
pickSoftThreshold.fromSimilarity(
    similarity,
    RsquaredCut = 0.85,
    powerVector = c(seq(1, 10, by = 1), seq(12, 20, by = 2)),
    removeFirst = FALSE, nBreaks = 10, blockSize = 1000,
    moreNetworkConcepts=FALSE,
    verbose = 0, indent = 0)
```

Arguments

data	expression data in a matrix or data frame. Rows correspond to samples and columns to genes.
dataIsExpr	logical: should the data be interpreted as expression (or other numeric) data, or as a similarity matrix of network nodes?
weights	optional observation weights for data to be used in correlation calculation. A matrix of the same dimensions as datExpr, containing non-negative weights. Only used with Pearson correlation.
similarity	similarity matrix: a symmetric matrix with entries between 0 and 1 and unit diagonal. The only transformation applied to similarity is raising it to a power.
RsquaredCut	desired minimum scale free topology fitting index \mathbb{R}^2 .
powerVector	a vector of soft thresholding powers for which the scale free topology fit indices are to be calculated.

298 pickSoftThreshold

removeFirst should the first bin be removed from the connectivity histogram?

nBreaks number of bins in connectivity histograms

blockSize block size into which the calculation of connectivity should be broken up. If not

given, a suitable value will be calculated using function blockSize and printed

if verbose>0. If R runs into memory problems, decrease this value.

corFnc the correlation function to be used in adjacency calculation.

corOptions a list giving further options to the correlation function specified in corFnc.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

moreNetworkConcepts

logical: should additional network concepts be calculated? If TRUE, the function will calculate how the network density, the network heterogeneity, and the network centralization depend on the power. For the definition of these additional

network concepts, see Horvath and Dong (2008). PloS Comp Biol.

gcInterval a number specifying in interval (in terms of individual genes) in which garbage

collection will be performed. The actual interval will never be less than blockSize.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The function calculates weighted networks either by interpreting data directly as similarity, or first transforming it to similarity of the type specified by networkType. The weighted networks are obtained by raising the similarity to the powers given in powerVector. For each power the scale free topology fit index is calculated and returned along with other information on connectivity.

On systems with multiple cores or processors, the function pickSoftThreshold takes advantage of parallel processing if the function enableWGCNAThreads has been called to allow parallel processing and set up the parallel calculation back-end.

Value

A list with the following components:

powerEstimate estimate of an appropriate soft-thresholding power: the lowest power for which

the scale free topology fit \mathbb{R}^2 exceeds RsquaredCut. If \mathbb{R}^2 is below RsquaredCut

for all powers, NA is returned.

fitIndices a data frame containing the fit indices for scale free topology. The columns

contain the soft-thresholding power, adjusted \mathbb{R}^2 for the linear fit, the linear coefficient, adjusted \mathbb{R}^2 for a more complicated fit models, mean connectivity, median connectivity and maximum connectivity. If input moreNetworkConcepts is TRUE, 3 additional columns containing network density, centralization, and

heterogeneity.

Author(s)

Steve Horvath and Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

See Also

```
adjacency, softConnectivity
```

```
plotClusterTreeSamples
```

Annotated clustering dendrogram of microarray samples

Description

This function plots an annotated clustering dendorgram of microarray samples.

Usage

```
plotClusterTreeSamples(
  datExpr,
  y = NULL,
  traitLabels = NULL,
  yLabels = NULL,
  main = if (is.null(y)) "Sample dendrogram" else
                         "Sample dendrogram and trait indicator",
  setLayout = TRUE, autoColorHeight = TRUE, colorHeight = 0.3,
  dendroLabels = NULL,
  addGuide = FALSE, guideAll = TRUE,
  guideCount = NULL, guideHang = 0.2,
  cex.traitLabels = 0.8,
  cex.dendroLabels = 0.9,
  marAll = c(1, 5, 3, 1),
  saveMar = TRUE,
  abHeight = NULL, abCol = "red",
  ...)
```

Arguments

datExpr a data frame containing expression data, with rows corresponding to samples

and columns to genes. Missing values are allowed and will be ignored.

y microarray sample trait. Either a vector with one entry per sample, or a matrix in

which each column corresponds to a (different) trait and each row to a sample.

traitLabels labels to be printed next to the color rows depicting sample traits. Defaults to

column names of y.

yLabels Optional labels to identify colors in the row identifying the sample classes. If

given, must be of the same dimensions as y. Each label that occurs will be

displayed once.

main title for the plot.

setLayout logical: should the plotting device be partitioned into a standard layout? If

FALSE, the user is responsible for partitioning. The function expects two regions

of the same width, the first one immediately above the second one.

autoColorHeight

logical: should the height of the color area below the dendrogram be automati-

cally adjusted for the number of traits? Only effective if setLayout is TRUE.

colorHeight Specifies the height of the color area under dendrogram as a fraction of the

 $height\ of\ the\ dendrogram\ area.\ Only\ effective\ when\ \verb"autoColorHeight" above\ is$

FALSE.

dendroLabels dendrogram labels. Set to FALSE to disable dendrogram labels altogether; set to

NULL to use row labels of datExpr.

addGuide logical: should vertical "guide lines" be added to the dendrogram plot? The

lines make it easier to identify color codes with individual samples.

guideAll logical: add a guide line for every sample? Only effective for addGuide set

TRUE.

guideCount number of guide lines to be plotted. Only effective when addGuide is TRUE and

guideAll is FALSE.

guideHang fraction of the dendrogram height to leave between the top end of the guide line

and the dendrogram merge height. If the guide lines overlap with dendrogram

labels, increase guideHang to leave more space for the labels.

cex.traitLabels

character expansion factor for trait labels.

cex.dendroLabels

character expansion factor for dendrogram (sample) labels.

marAll a 4-element vector giving the bottom, left, top and right margins around the

combined plot. Note that this is not the same as setting the margins via a call to par, because the bottom margin of the dendrogram and the top margin of the

color underneath are always zero.

saveMar logical: save margins setting before starting the plot and restore on exit?

abHeight optional specification of the height for a horizontal line in the dendrogram, see

abline.

abCol color for plotting the horizontal line.

.. other graphical parameters to plot.hclust.

plotColorUnderTree 301

Details

The function generates an average linkage hierarchical clustering dendrogram (see hclust) of samples from the given expression data, using Eclidean distance of samples. The dendrogram is plotted together with color annotation for the samples.

The trait y must be numeric. If y is integer, the colors will correspond to values. If y is continouos, it will be dichotomized to two classes, below and above median.

Value

None.

Author(s)

Steve Horvath and Peter Langfelder

See Also

dist, hclust, plotDendroAndColors

plotColorUnderTree

Plot color rows in a given order, for example under a dendrogram

Description

Plot color rows encoding information about objects in a given order, for example the order of a clustering dendrogram, usually below the dendrogram or a barplot.

Usage

```
plotOrderedColors(
   order,
   colors,
   main = "",
   rowLabels = NULL,
   rowWidths = NULL,
   rowText = NULL,
   rowTextAlignment = c("left", "center", "right"),
   rowTextIgnore = NULL,
   textPositions = NULL,
   addTextGuide = TRUE,
   cex.rowLabels = 1,
   cex.rowText = 0.8,
   startAt = 0,
   align = c("center", "edge"),
   separatorLine.col = "black",
   ...)
```

302 plotColorUnderTree

```
plotColorUnderTree(
    dendro,
    colors,
    rowLabels = NULL,
    rowText = NULL,
    rowTextAlignment = c("left", "center", "right"),
    rowTextIgnore = NULL,
    textPositions = NULL,
    addTextGuide = TRUE,
    cex.rowLabels = 1,
    cex.rowText = 0.8,
    separatorLine.col = "black",
    ...)
```

Arguments

order A vector giving the order of the objects. Must have the same length as colors if

colors is a vector, or as the number of rows if colors is a matrix or data frame.

dendro A hierarchical clustering dendrogram such one returned by hclust.

colors Coloring of objects on the dendrogram. Either a vector (one color per object)

or a matrix (can also be an array or a data frame) with each column giving one color per object. Each column will be plotted as a horizontal row of colors under

the dendrogram.

main Optional main title.

rowLabels Labels for the colorings given in colors. The labels will be printed to the left of

the color rows in the plot. If the argument is given, it must be a vector of length equal to the number of columns in colors. If not given, names(colors) will be used if available. If not, sequential numbers starting from 1 will be used.

rowWidths Optional specification of relative row widths for the color and text (if given)

rows. Need not sum to 1.

rowText Optional labels to identify colors in the color rows. If given, must be of the same

dimensions as colors. Each label that occurs will be displayed once.

rowTextAlignment

Character string specifying whether the labels should be left-justified to the start of the largest block of each label, centered in the middle, or right-justified to the

end of the largest block.

rowTextIgnore Optional specifications of labels that should be ignored when displaying them

using rowText above.

textPositions optional numeric vector of the same length as the number of columns in rowText

giving the color rows under which the text rows should appear.

addTextGuide logical: should guide lines be added for the text rows (if given)?

cex.rowLabels Font size scale factor for the row labels. See par.
cex.rowText character expansion factor for text rows (if given).

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startAt A numeric value indicating where in relationship to the left edge of the plot the

center of the first rectangle should be. Useful values are 0 if ploting color under

a dendrogram, and 0.5 if ploting colors under a barplot.

align Controls the alignment of the color rectangles. "center" means aligning centers

of the rectangles on equally spaced values; "edge" means aligning edges of the

first and last rectangles on the edges of the plot region.

separatorLine.col

Color of the line separating rows of color rectangles. If NA, no lines will be

drawn.

.. Other parameters to be passed on to the plotting method (such as main for the

main title etc).

Details

It is often useful to plot dendrograms or other plots (e.g., barplots) of objects together with additional information about the objects, for example module assignment (by color) that was obtained by cutting a hierarchical dendrogram or external color-coded measures such as gene significance. This function provides a way to do so. The calling code should section the screen into two (or more) parts, plot the dendrogram (via plot(hclust)) or other information in the upper section and use this function to plot color annotation in the order corresponding to the dendrogram in the lower section.

Value

A list with the following components

colorRectangles

A list with one component per color row. Each component is a list with 4 elements x1, yb, xr, yt giving the left, bottom, right and top coordinates of the rectangles in that row.

Note

This function replaces plotHclustColors in package moduleColor.

Author(s)

Steve Horvath <SHorvath@mednet.ucla.edu> and Peter Langfelder <Peter.Langfelder@gmail.com>

See Also

cutreeDynamic for module detection in a dendrogram;

plotDendroAndColors for automated plotting of dendrograms and colors in one step.

304 plotCor

plotCor	Red and Green Color Image of Correlation Matrix

Description

This function produces a red and green color image of a correlation matrix using an RGB color specification. Increasingly positive correlations are represented with reds of increasing intensity, and increasingly negative correlations are represented with greens of increasing intensity.

Usage

```
plotCor(x, new=FALSE, nrgcols=50, labels=FALSE, labcols=1, title="", ...)
```

Arguments

x	a matrix of numerical values.
new	If new=F, x must already be a correlation matrix. If new=T, the correlation matrix for the columns of x is computed and displayed in the image.
nrgcols	the number of colors (>= 1) to be used in the red and green palette.
labels	vector of character strings to be placed at the tickpoints, labels for the columns of \boldsymbol{x} .
labcols	colors to be used for the labels of the columns of x . labcols can have either length 1, in which case all the labels are displayed using the same color, or the same length as labels, in which case a color is specified for the label of each column of x .
title	character string, overall title for the plot.
	graphical parameters may also be supplied as arguments to the function (see par). For comparison purposes, it is good to set $zlim=c(-1,1)$.

Author(s)

Sandrine Dudoit, <sandrine@stat.berkeley.edu>

See Also

```
plotMat,rgcolors.func, cor, image, rgb.
```

plotDendroAndColors 305

plotDendroAndColors

Dendrogram plot with color annotation of objects

Description

This function plots a hierarchical clustering dendrogram and color annotation(s) of objects in the dendrogram underneath.

Usage

```
plotDendroAndColors(
  dendro,
  colors,
  groupLabels = NULL,
  rowText = NULL,
  rowTextAlignment = c("left", "center", "right"),
  rowTextIgnore = NULL,
  textPositions = NULL,
  setLayout = TRUE,
  autoColorHeight = TRUE,
  colorHeight = 0.2,
  colorHeightBase = 0.2,
  colorHeightMax = 0.6,
  rowWidths = NULL,
  dendroLabels = NULL,
  addGuide = FALSE, guideAll = FALSE,
  guideCount = 50, guideHang = 0.2,
  addTextGuide = FALSE,
  cex.colorLabels = 0.8, cex.dendroLabels = 0.9,
  cex.rowText = 0.8,
  marAll = c(1, 5, 3, 1), saveMar = TRUE,
  abHeight = NULL, abCol = "red", ...)
```

Arguments

dendro

colors	Coloring of objects on the dendrogram. Either a vector (one color per object)
	or a matrix (can also be an array or a data frame) with each column giving one
	color per object. Each column will be plotted as a horizontal row of colors under
	the dendrogram.

a hierarchical clustering dendrogram such as one produced by hclust.

the dendrogram.

groupLabels Labels for the colorings given in colors. The labels will be printed to the left of

the color rows in the plot. If the argument is given, it must be a vector of length equal to the number of columns in colors. If not given, names(colors) will be used if available. If not, sequential numbers starting from 1 will be used.

rowText Optional labels to identify colors in the color rows. If given, must be either

the same dimensions as colors or must have the same number of rows and

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> textPositions must be used to specify which columns of colors each column of rowText corresponds to. Each label that occurs will be displayed once, under the largest continuous block of the corresponding colors.

rowTextAlignment

Character string specifying whether the labels should be left-justified to the start of the largest block of each label, centered in the middle, or right-justified to the end of the largest block.

rowTextIgnore Optional specifications of labels that should be ignored when displaying them using rowText above.

> optional numeric vector of the same length as the number of columns in rowText giving the color rows under which the text rows should appear.

logical: should the plotting device be partitioned into a standard layout? If FALSE, the user is responsible for partitioning. The function expects two regions of the same width, the first one immediately above the second one.

autoColorHeight

textPositions

setLayout

logical: should the height of the color area below the dendrogram be automatically adjusted for the number of traits? Only effective if setLayout is TRUE.

specifies the height of the color area under dendrogram as a fraction of the height colorHeight of the dendrogram area. Only effective when autoColorHeight above is FALSE.

colorHeightBase

addGuide

guideHang

when autoColorHeight is TRUE, this specifies the minimum height of the color area (the height when there is one color row).

when autoColorHeight is TRUE, this specifies the maximum height of the color colorHeightMax area (the height when there are many color rows).

optional specification of relative row widths for the color and text (if given) rowWidths rows. Need not sum to 1.

dendroLabels dendrogram labels. Set to FALSE to disable dendrogram labels altogether; set to NULL to use row labels of datExpr.

> logical: should vertical "guide lines" be added to the dendrogram plot? The lines make it easier to identify color codes with individual samples.

logical: add a guide line for every sample? Only effective for addGuide set guideAll

number of guide lines to be plotted. Only effective when addGuide is TRUE and

guideCount guideAll is FALSE.

> fraction of the dendrogram height to leave between the top end of the guide line and the dendrogram merge height. If the guide lines overlap with dendrogram labels, increase guideHang to leave more space for the labels.

addTextGuide logical: should guide lines be added for the text rows (if given)? cex.colorLabels

character expansion factor for trait labels.

cex.dendroLabels

character expansion factor for dendrogram (sample) labels.

cex.rowText character expansion factor for text rows (if given).

marAll	a vector of length 4 giving the bottom, left, top and right margins of the combined plot. There is no margin between the dendrogram and the color plot underneath.
saveMar	logical: save margins setting before starting the plot and restore on exit?
abHeight	optional specification of the height for a horizontal line in the dendrogram, see abline.
abCol	color for plotting the horizontal line.
	other graphical parameters to plot.hclust.

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Details

The function slits the plotting device into two regions, plots the given dendrogram in the upper region, then plots color rows in the region below the dendrogram.

Value

None.

Author(s)

Peter Langfelder

See Also

plotColorUnderTree

```
plotEigengeneNetworks Eigengene network plot
```

Description

This function plots dendrogram and eigengene representations of (consensus) eigengenes networks. In the case of conensus eigengene networks the function also plots pairwise preservation measures between consensus networks in different sets.

Usage

```
plotEigengeneNetworks(
   multiME,
   setLabels,
   letterSubPlots = FALSE, Letters = NULL,
   excludeGrey = TRUE, greyLabel = "grey",
   plotDendrograms = TRUE, plotHeatmaps = TRUE,
   setMargins = TRUE, marDendro = NULL, marHeatmap = NULL,
   colorLabels = TRUE, signed = TRUE,
   heatmapColors = NULL,
   plotAdjacency = TRUE,
```

```
printAdjacency = FALSE, cex.adjacency = 0.9,
coloredBarplot = TRUE, barplotMeans = TRUE, barplotErrors = FALSE,
plotPreservation = "standard",
zlimPreservation = c(0, 1),
printPreservation = FALSE, cex.preservation = 0.9,
...)
```

Arguments

multiME either a single data frame containing the module eigengenes, or module eigen-

genes in the multi-set format (see checkSets). The multi-set format is a vector of lists, one per set. Each set must contain a component data whose rows cor-

respond to samples and columns to eigengenes.

setLabels A vector of character strings that label sets in multiME.

letterSubPlots logical: should subplots be lettered?

Letters optional specification of a sequence of letters for lettering. Defaults to "ABCD"...

excludeGrey logical: should the grey module eigengene be excluded from the plots?

greyLabel label for the grey module. Usually either "grey" or the number 0.

plotDendrograms

logical: should eigengene dendrograms be plotted?

plotHeatmaps logical: should eigengene network heatmaps be plotted?

setMargins logical: should margins be set? See par.

marDendro a vector of length 4 giving the margin setting for dendrogram plots. See par.

If setMargins is TRUE and marDendro is not given, the function will provide

reasonable default values.

marHeatmap a vector of length 4 giving the margin setting for heatmap plots. See par. If

setMargins is TRUE and marDendro is not given, the function will provide rea-

sonable default values.

colorLabels logical: should module eigengene names be interpreted as color names and the

colors used to label heatmap plots and barplots?

signed logical: should eigengene networks be constructed as signed?

heatmapColors color palette for heatmaps. Defaults to heat.colors when signed is FALSE,

and to redWhiteGreen when signed is TRUE.

plotAdjacency logical: should module eigengene heatmaps plot adjacency (ranging from 0 to

1), or correlation (ranging from -1 to 1)?

printAdjacency logical: should the numerical values be printed into the adjacency or correlation

heatmap?

cex.adjacency character expansion factor for printing of numerical values into the adjacency or

correlation heatmap

coloredBarplot logical: should the barplot of eigengene adjacency preservation distinguish in-

dividual contributions by color? This is possible only if colorLabels is TRUE

and module eigengene names encode valid colors.

barplotMeans logical: plot mean preservation in the barplot? This option effectively rescales

the preservation by the number of eigengenes in the network. If means are

plotted, the barplot is not colored.

barplotErrors logical: should standard errors of the mean preservation be plotted?

plotPreservation

a character string specifying which type of preservation measure to plot. Allowed values are (unique abbreviations of) "standard", "hyperbolic", "both".

zlimPreservation

a vector of length 2 giving the value limits for the preservation heatmaps.

printPreservation

logical: should preservation values be printed within the heatmap?

cex.preservation

character expansion factor for preservation display.

... other graphical arguments to function labeledHeatmap.

Details

Consensus eigengene networks consist of a fixed set of eigengenes "expressed" in several different sets. Network connection strengths are given by eigengene correlations. This function aims to visualize the networks as well as their similarities and differences across sets.

The function partitions the screen appropriately and plots eigengene dendrograms in the top row, then a square matrix of plots: heatmap plots of eigengene networks in each set on the diagonal, heatmap plots of pairwise preservation networks below the diagonal, and barplots of aggregate network preservation of individual eigengenes above the diagonal. A preservation plot or barplot in the row i and column j of the square matrix represents the preservation between sets i and j.

Individual eigengenes are labeled by their name in the dendrograms; in the heatmaps and barplots they can optionally be labeled by color squares. For compatibility with other functions, the color labels are encoded in the eigengene names by prefixing the color with two letters, such as "MEturquoise".

Two types of network preservation can be plotted: the "standard" is simply the difference between adjacencies in the two compared sets. The "hyperbolic" difference de-emphasizes the preservation of low adjacencies. When "both" is specified, standard preservation is plotted in the lower triangle and hyperbolic in the upper triangle of each preservation heatmap.

If the eigengenes are labeled by color, the bars in the barplot can be split into segments representing the contribution of each eigengene and labeled by the contribution. For example, a yellow segment in a bar labeled by a turquoise square represents the preservation of the adjacency between the yellow and turquoise eigengenes in the two networks compared by the barplot.

For large numbers of eigengenes and/or sets, it may be difficult to get a meaningful plot fit a standard computer screen. In such cases we recommend using a device such as postscript or pdf where the user can specify large dimensions; such plots can be conveniently viewed in standard pdf or postscript viewers.

Value

None.

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Author(s)

Peter Langfelder

References

For theory and applications of consensus eigengene networks, see

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

labeledHeatmap, labeledBarplot for annotated heatmaps and barplots; hclust for hierarchical clustering and dendrogram plots

plotMat

Red and Green Color Image of Data Matrix

Description

This function produces a red and green color image of a data matrix using an RGB color specification. Larger entries are represented with reds of increasing intensity, and smaller entries are represented with greens of increasing intensity.

Usage

```
plotMat(x, nrgcols=50, rlabels=FALSE, clabels=FALSE, rcols=1, ccols=1, title="",...)
```

Arguments

X	a matrix of numbers.
nrgcols	the number of colors (>= 1) to be used in the red and green palette.
rlabels	vector of character strings to be placed at the row tickpoints, labels for the rows of x.
clabels	vector of character strings to be placed at the column tickpoints, labels for the columns of x.
rcols	colors to be used for the labels of the rows of x. rcols can have either length 1, in which case all the labels are displayed using the same color, or the same length as rlabels, in which case a color is specified for the label of each row of x.
ccols	colors to be used for the labels of the columns of x. ccols can have either length 1, in which case all the labels are displayed using the same color, or the same length as clabels, in which case a color is specified for the label of each column of x.
title	character string, overall title for the plot.
	graphical parameters may also be supplied as arguments to the function (see par). E.g. $zlim=c(-3,3)$

plotMEpairs 311

Author(s)

Sandrine Dudoit, <sandrine@stat.berkeley.edu>

See Also

```
plotCor, rgcolors.func, cor, image, rgb.
```

plotMEpairs

Pairwise scatterplots of eigengenes

Description

The function produces a matrix of plots containing pairwise scatterplots of given eigengenes, the distribution of their values and their pairwise correlations.

Usage

```
plotMEpairs(
   datME,
   y = NULL,
   main = "Relationship between module eigengenes",
   clusterMEs = TRUE,
   ...)
```

Arguments

datME a data frame containing expression data, with rows corresponding to samples and columns to genes. Missing values are allowed and will be ignored.

y optional microarray sample trait vector. Will be treated as an additional eigen-

gene.

main title for the plot.

clusterMEs logical: should the module eigengenes be ordered by their dendrogram?

... additional graphical parameters to the function pairs

Details

The function produces an NxN matrix of plots, where N is the number of eigengenes. In the upper traingle it plots pairwise scatterplots of module eigengenes (plus the trait y, if given). On the diagonal it plots histograms of sample values for each eigengene. Below the diagonal, it displays the pairwise correlations of the eigengenes.

Value

None.

Author(s)

Steve Horvath

See Also

pairs

```
plotModuleSignificance
```

Barplot of module significance

Description

Plot a barplot of gene significance.

Usage

```
plotModuleSignificance(
   geneSignificance,
   colors,
   boxplot = FALSE,
   main = "Gene significance across modules,",
   ylab = "Gene Significance", ...)
```

Arguments

geneSignificance

a numeric vector giving gene significances.

colors a character vector specifying module assignment for the genes whose signifi-

cance is given in geneSignificance. The modules should be labeled by col-

ors.

boxplot logical: should a boxplot be produced instead of a barplot?

main main title for the plot.

ylab y axis label for the plot.

... other graphical parameters to plot.

Details

Given individual gene significances and their module assignment, the function calculates the module significance for each module as the average gene significance of the genes within the module. The result is plotted in a barplot or boxplot form. Each bar or box is labeled by the corresponding module color.

Value

None.

plotMultiHist 313

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

See Also

barplot, boxplot

plotMultiHist

Plot multiple histograms in a single plot

Description

This function plots density or cumulative distribution function of multiple histograms in a single plot, using lines.

Usage

```
plotMultiHist(
   data,
   nBreaks = 100,
   col = 1:length(data),
   scaleBy = c("area", "max", "none"),
   cumulative = FALSE,
   ...)
```

Arguments

data	A list in which each component corresponds to a separate histogram and is a vector of values to be shown in each histogram.
nBreaks	Number of breaks in the combined plot.
col	Color of the lines. Should be a vector of the same length as data.
scaleBy	Method to make the different histograms comparable. The counts are scaled such that either the total area or the maximum are the same for all histograms, or the histograms are shown without scaling.
cumulative	Logical: should the cumulative distribution be shown instead of the density?
	Other graphical arguments.

plotNetworkHeatmap

Value

Invisibly,

x A list with one component per histogram (component of data), giving the bin

midpoints

y A list with one component per histogram (component of data), giving the scaled

bin counts

Note

This function is still experimental and behavior may change in the future.

Author(s)

Peter Langfelder

See Also

hist

Examples

```
data = list(rnorm(1000), rnorm(10000) + 2);
plotMultiHist(data, xlab = "value", ylab = "scaled density")
```

plotNetworkHeatmap

Network heatmap plot

Description

Network heatmap plot.

Usage

```
plotNetworkHeatmap(
  datExpr,
  plotGenes,
  weights = NULL,
  useTOM = TRUE,
  power = 6,
  networkType = "unsigned",
  main = "Heatmap of the network")
```

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Arguments

datExpr a data frame containing expression data, with rows corresponding to samples

and columns to genes. Missing values are allowed and will be ignored.

plotGenes a character vector giving the names of genes to be included in the plot. The

names will be matched against names (datExpr).

weights optional observation weights for datExpr to be used in correlation calculation.

A matrix of the same dimensions as datExpr, containing non-negative weights.

Only used with Pearson correlation.

useTOM logical: should TOM be plotted (TRUE), or correlation-based adjacency (FALSE)?

power soft-thresholding power for network construction.

networkType a character string giving the newtork type. Recognized values are (unique ab-

breviations of) "unsigned", "signed", and "signed hybrid".

main main title for the plot.

Details

The function constructs a network from the given expression data (selected by plotGenes) using the soft-thresholding procedure, optionally calculates Topological Overlap (TOM) and plots a heatmap of the network.

Note that all network calculations are done in one block and may fail due to memory allocation issues for large numbers of genes.

Value

None.

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

adjacency, TOMsimilarity

populationMeansInAdmixture

Estimate the population-specific mean values in an admixed population.

Description

Uses the expression values from an admixed population and estimates of the proportions of subpopulations to estimate the population specific mean values. For example, this function can be used to estimate the cell type specific mean gene expression values based on expression values from a mixture of cells. The method is described in Shen-Orr et al (2010) where it was used to estimate cell type specific gene expression levels based on a mixture sample.

Usage

```
populationMeansInAdmixture(
   datProportions, datE.Admixture,
   scaleProportionsTo1 = TRUE,
   scaleProportionsInCelltype = TRUE,
   setMissingProportionsToZero = FALSE)
```

Arguments

datProportions a matrix of non-negative numbers (ideally proportions) where the rows correspond to the samples (rows of datE. Admixture) and the columns correspond to the sub-populations of the mixture. The function calculates a mean expression value for each column of datProportions. Negative entries in datProportions lead to an error message. But the rows of datProportions do not have to sum to 1, see the argument scaleProportionsTo1.

datE. Admixture a matrix of numbers. The rows correspond to samples (mixtures of populations). The columns contain the variables (e.g. genes) for which the means should be estimated.

scaleProportionsTo1

logical. If set to TRUE (default) then the proportions in each row of datProportions are scaled so that they sum to 1, i.e. datProportions[i,]=datProportions[i,]/max(datProportions[i,]). In general, we recommend to set it to TRUE.

scaleProportionsInCelltype

logical. If set to TRUE (default) then the proportions in each cell types are recaled and make the mean to 0.

setMissingProportionsToZero

logical. Default is FALSE. If set to TRUE then it sets missing values in datProportions

Details

The function outputs a matrix of coefficients resulting from fitting a regression model. If the proportions sum to 1, then i-th row of the output matrix reports the coefficients of the following model lm(datE.Admixture[,i]~.-1, data=datProportions). Aside, the minus 1 in the formula indicates that no intercept term will be fit. Under certain assumptions, the coefficients can be interpreted as the mean expression values in the sub-populations (Shen-Orr 2010).

Value

a numeric matrix whose rows correspond to the columns of datE.Admixture (e.g. to genes) and whose columns correspond to the columns of datProportions (e.g. sub populations or cell types).

Note

This can be considered a wrapper of the 1m function.

Author(s)

Steve Horvath, Chaochao Cai

References

Shen-Orr SS, Tibshirani R, Khatri P, Bodian DL, Staedtler F, Perry NM, Hastie T, Sarwal MM, Davis MM, Butte AJ (2010) Cell type-specific gene expression differences in complex tissues. Nature Methods, vol 7 no.4

Examples

```
set.seed(1)
# this is the number of complex (mixed) tissue samples, e.g. arrays
# true count data (e.g. pure cells in the mixed sample)
datTrueCounts=as.matrix(data.frame(TrueCount1=rpois(m,lambda=16),
TrueCount2=rpois(m,lambda=8),TrueCount3=rpois(m,lambda=4),
TrueCount4=rpois(m,lambda=2)))
no.pure=dim(datTrueCounts)[[2]]
# now we transform the counts into proportions
divideBySum=function(x) t(x)/sum(x)
datProportions= t(apply(datTrueCounts,1,divideBySum))
dimnames(datProportions)[[2]]=paste("TrueProp",1:dim(datTrueCounts)[[2]],sep=".")
# number of genes that are highly expressed in each pure population
no.genesPerPure=rep(5, no.pure)
no.genes= sum(no.genesPerPure)
GeneIndicator=rep(1:no.pure, no.genesPerPure)
# true mean values of the genes in the pure populations
# in the end we hope to estimate them from the mixed samples
datTrueMeans0=matrix( rnorm(no.genes*no.pure,sd=.3), nrow= no.genes,ncol=no.pure)
for (i in 1:no.pure ){
datTrueMeans0[GeneIndicator==i,i]= datTrueMeans0[GeneIndicator==i,i]+1
dimnames(datTrueMeans0)[[1]]=paste("Gene",1:dim(datTrueMeans0)[[1]],sep="." )
dimnames(datTrueMeans0)[[2]]=paste("MeanPureCellType",1:dim(datTrueMeans0)[[2]],
                                   sep=".")
```

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```
# plot.mat(datTrueMeans0)
# simulate the (expression) values of the admixed population samples
noise=matrix(rnorm(m*no.genes,sd=.1),nrow=m,ncol= no.genes)
datE.Admixture= as.matrix(datProportions) %*% t(datTrueMeans0) + noise
dimnames(datE.Admixture)[[1]]=paste("MixedTissue",1:m,sep=".")
datPredictedMeans=populationMeansInAdmixture(datProportions,datE.Admixture)
par(mfrow=c(2,2))
for (i in 1:4){
verboseScatterplot(datPredictedMeans[,i],datTrueMeans0[,i],
xlab="predicted mean",ylab="true mean",main="all populations")
abline(0,1)
}
#assume we only study 2 populations (ie we ignore the others)
selectPopulations=c(1,2)
dat Predicted Means Too Few=population Means In Admixture (dat Proportions [, select Populations], and the proportion of the proportion 
                                                                                                                                 datE.Admixture)
par(mfrow=c(2,2))
for (i in 1:length(selectPopulations) ){
verbose Scatterplot(dat Predicted Means Too Few[,i], dat True Means 0[,i],\\
xlab="predicted mean",ylab="true mean",main="too few populations")
abline(0,1)
}
#assume we erroneously add a population
\label{lem:datProportions} dat Proportions, \\ \mbox{$W$rongProp$=sample(datProportions[,1]))$}
datPredictedMeansTooMany=populationMeansInAdmixture(datProportionsTooMany, datPredictedMeansTooMany)
                                                                                   datE.Admixture)
par(mfrow=c(2,2))
for (i in 1:4){
    verboseScatterplot(datPredictedMeansTooMany[,i],datTrueMeans0[,i],
    xlab="predicted mean",ylab="true mean",main="too many populations")
    abline(0,1)
}
```

pquantile

Parallel quantile, median, mean

Description

Calculation of "parallel" quantiles, minima, maxima, medians, and means, across given arguments or across lists

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Usage

```
pquantile(prob, ...)
pquantile.fromList(dataList, prob)
pmedian(...)
pmean(..., weights = NULL)
pmean.fromList(dataList, weights = NULL)
pminWhich.fromList(dataList)
```

Arguments

prob	A single probability at which to calculate the quantile. See quantile.
dataList	A list of numeric vectors or arrays, all of the same length and dimensions, over which to calculate "parallel" quantiles.
weights	Optional vector of the same length as dataList, giving the weights to be used in the weighted mean. If not given, unit weights will be used.
	Numeric arguments. All arguments must have the same dimensions. See details.

Details

Given numeric arguments, say x,y,z, of equal dimensions (and length), the pquantile calculates and returns the quantile of the first components of x,y,z, then the second components, etc. Similarly, pmedian and pmean calculate the median and mean, respectively. The funtion pquantile from List is identical to pquantile except that the argument dataList replaces the ... in holding the numeric vectors over which to calculate the quantiles.

Value

Dimensions are copied from dimensions of the input arguments. If any of the input variables have dimnames, the first non-NULL dimnames are copied into the output.

Author(s)

Peter Langfelder and Steve Horvath

See Also

```
quantile, median, mean for the underlying statistics.
```

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Examples

```
# Generate 2 simple matrices
a = matrix(c(1:12), 3, 4);
b = a+ 1;
c = a + 2;

# Set the colnames on matrix a

colnames(a) = spaste("col_", c(1:4));

# Example use

pquantile(prob = 0.5, a, b, c)

pmean(a,b,c)
pmedian(a,b,c)
```

prepComma

Prepend a comma to a non-empty string

Description

Utility function that prepends a comma before the input string if the string is non-empty.

Usage

```
prepComma(s)
```

Arguments

S

Character string.

Value

If s is non-empty, returns paste(", ", s), otherwise returns s.

Author(s)

Peter Langfelder

Examples

```
prepComma("abc");
prepComma("");
```

prependZeros 321

prependZeros	Pad numbers with leading zeros to specified total width

Description

These functions pad the specified numbers with zeros to a specified total width.

Usage

```
prependZeros(x, width = max(nchar(x)))
prependZeros.int(x, width = max(nchar(as.integer(x))))
```

Arguments

x Vector of numbers to be padded. For prependZeros, the vector may be real

(non-integer) or even character (and not necessarily representing numbers). For prependZeros, the vector must be numeric and non-integers get rounded down

to the nearest integer.

width Width to pad the numbers to.

Details

The prependZeros.int version works better with numbers such as 100000 which may get converted to character as 1e5 and hence be incorrectly padded in the prependZeros function. On the flip side, prependZeros works also for non-integer inputs.

Value

Character vector with the 0-padded numbers.

Author(s)

Peter Langfelder

Examples

```
prependZeros(1:10)
prependZeros(1:10, 4)
# more exotic examples
prependZeros(c(1, 100000), width = 6) ### Produces incorrect output
prependZeros.int(c(1, 100000)) ### Correct output
prependZeros(c("a", "b", "aa")) ### pads the shorter strings using zeros.
```

```
preservationNetworkConnectivity
```

Network preservation calculations

Description

This function calculates several measures of gene network preservation. Given gene expression data in several individual data sets, it calculates the individual adjacency matrices, forms the preservation network and finally forms several summary measures of adjacency preservation for each node (gene) in the network.

Usage

```
preservationNetworkConnectivity(
   multiExpr,
   useSets = NULL, useGenes = NULL,
   corFnc = "cor", corOptions = "use='p'",
   networkType = "unsigned",
   power = 6,
   sampleLinks = NULL, nLinks = 5000,
   blockSize = 1000,
   setSeed = 12345,
   weightPower = 2,
   verbose = 2, indent = 0)
```

Arguments

multiExpr	expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.
useSets	optional specification of sets to be used for the preservation calculation. Defaults to using all sets.
useGenes	optional specification of genes to be used for the preservation calculation. Defaults to all genes.
corFnc	character string containing the name of the function to calculate correlation. Suggested functions include "cor" and "bicor".
corOptions	further argument to the correlation function.
networkType	a character string encoding network type. Recognized values are (unique abbreviations of) "unsigned", "signed", and "signed hybrid".
power	soft thresholding power for network construction. Should be a number greater than $1.$
sampleLinks	logical: should network connections be sampled (TRUE) or should all connections be used systematically (FALSE)?

nLinks number of links to be sampled. Should be set such that nLinks * nNeighbors

be several times larger than the number of genes.

blockSize correlation calculations will be split into square blocks of this size, to prevent

running out of memory for large gene sets.

setSeed seed to be used for sampling, for repeatability. If a seed already exists, it is saved

before the sampling starts and restored upon exit.

weightPower power with which higher adjacencies will be weighted in weighted means

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The preservation network is formed from adjacencies of compared sets. For 'complete' preservations, all given sets are compared at once; for 'pairwise' preservations, the sets are compared in pairs. Unweighted preservations are simple mean preservations for each node; their weighted counterparts are weighted averages in which a preservation of adjacencies $A_{ij}^{(1)}$ and $A_{ij}^{(2)}$ of nodes i, jbetween sets 1 and 2 is weighted by $[(A_{ij}^{(1)} + A_{ij}^{(2)})/2]^w eightPower$. The hyperbolic preservation is based on $tanh[(max - min)/(max + min)^2]$, where max and min are the componentwise maximum and minimum of the compared adjacencies, respectively.

Value

A list with the following components:

a matrix with rows corresponding to genes and columns to unique pairs of given pairwise

sets, giving the pairwise preservation of the adjacencies connecting the gene to

all other genes.

complete a vector with one entry for each input gene containing the complete mean preser-

vation of the adjacencies connecting the gene to all other genes.

pairwiseWeighted

a matrix with rows corresponding to genes and columns to unique pairs of given sets, giving the pairwise weighted preservation of the adjacencies connecting

the gene to all other genes.

completeWeighted

a vector with one entry for each input gene containing the complete weighted

mean preservation of the adjacencies connecting the gene to all other genes.

pairwiseHyperbolic

a matrix with rows corresponding to genes and columns to unique pairs of given sets, giving the pairwise hyperbolic preservation of the adjacencies connecting

the gene to all other genes.

completeHyperbolic

a vector with one entry for each input gene containing the complete mean hyperbolic preservation of the adjacencies connecting the gene to all other genes.

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```
pairwiseWeightedHyperbolic
```

a matrix with rows corresponding to genes and columns to unique pairs of given sets, giving the pairwise weighted hyperbolic preservation of the adjacencies connecting the gene to all other genes.

```
completeWeightedHyperbolic
```

a vector with one entry for each input gene containing the complete weighted hyperbolic mean preservation of the adjacencies connecting the gene to all other genes.

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

adjacency for calculation of adjacency;

projectiveKMeans

Projective K-means (pre-)clustering of expression data

Description

Implementation of a variant of K-means clustering for expression data.

Usage

```
projectiveKMeans(
  datExpr,
  preferredSize = 5000,
  nCenters = as.integer(min(ncol(datExpr)/20, preferredSize^2/ncol(datExpr))),
  sizePenaltyPower = 4,
  networkType = "unsigned",
  randomSeed = 54321,
  checkData = TRUE,
  imputeMissing = TRUE,
  maxIterations = 1000,
  verbose = 0, indent = 0)
```

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Arguments

datExpr expression data. A data frame in which columns are genes and rows ar samples.

NAs are allowed, but not too many.

preferredSize preferred maximum size of clusters.

nCenters number of initial clusters. Empirical evidence suggests that more centers will

give a better preclustering; the default is an attempt to arrive at a reasonable

number.

sizePenaltyPower

parameter specifying how severe is the penalty for clusters that exceed preferredSize.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

randomSeed integer to be used as seed for the random number generator before the function

starts. If a current seed exists, it is saved and restored upon exit.

checkData logical: should data be checked for genes with zero variance and genes and

samples with excessive numbers of missing samples? Bad samples are ignored;

returned cluster assignment for bad genes will be NA.

imputeMissing logical: should missing values in datExpr be imputed before the calculations

start? The early imputation makes the code run faster but may produce slightly

different results if re-running older calculations.

maxIterations maximum iterations to be attempted.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The principal aim of this function within WGCNA is to pre-cluster a large number of genes into smaller blocks that can be handled using standard WGCNA techniques.

This function implements a variant of K-means clustering that is suitable for co-expression analysis. Cluster centers are defined by the first principal component, and distances by correlation (more precisely, 1-correlation). The distance between a gene and a cluster is multiplied by a factor of $max(clusterSize/preferredSize, 1)^{sizePenaltyPower}$, thus penalizing clusters whose size exceeds preferredSize. The function starts with randomly generated cluster assignment (hence the need to set the random seed for repeatability) and executes interations of calculating new centers and reassigning genes to nearest center until the clustering becomes stable. Before returning, nearby clusters are iteratively combined if their combined size is below preferredSize.

The standard principal component calculation via the function svd fails from time to time (likely a convergence problem of the underlying lapack functions). Such errors are trapped and the principal component is approximated by a weighted average of expression profiles in the cluster. If verbose is set above 2, an informational message is printed whenever this approximation is used.

Value

A list with the following components:

clusters A numerical vector with one component per input gene, giving the cluster num-

ber in which the gene is assigned.

centers Cluster centers, that is their first principal components.

Author(s)

Peter Langfelder

See Also

sizeRestrictedClusterMerge which implements the last step of merging smaller clusters.

proportionsInAdmixture

Estimate the proportion of pure populations in an admixed population based on marker expression values.

Description

Assume that datE. Admixture provides the expression values from a mixture of cell types (admixed population) and you want to estimate the proportion of each pure cell type in the mixed samples (rows of datE.Admixture). The function allows you to do this as long as you provide a data frame MarkerMeansPure that reports the mean expression values of markers in each of the pure cell types.

Usage

```
proportionsInAdmixture(
 MarkerMeansPure,
  datE.Admixture,
  calculateConditionNumber = FALSE,
  coefToProportion = TRUE)
```

Arguments

MarkerMeansPure

is a data frame whose first column reports the name of the marker and the remaining columns report the mean values of the markers in each of the pure populations. The function will estimate the proportion of pure cells which correspond to columns 2 through of dim(MarkerMeansPure)[[2]] of MarkerMeansPure. Rows that contain missing values (NA) will be removed.

datE. Admixture is a data frame of expression data, e.g. the columns of datE. Admixture could correspond to thousands of genes. The rows of datE. Admixture correspond to the admixed samples for which the function estimates the proportions of pure populations. Some of the markers specified in the first column of MarkerMeansPure should correspond to column names of datE.Admixture.

calculateConditionNumber

logical. Default is FALSE. If set to TRUE then it uses the kappa function to calculates the condition number of the matrix MarkerMeansPure[,-1]. This allows one to determine whether the linear model for estimating the proportions is well specified. Type help(kappa) to learn more. kappa() computes by default (an estimate of) the 2-norm condition number of a matrix or of the R matrix of a QR decomposition, perhaps of a linear fit.

coefToProportion

logical. By default, it is set to TRUE. When estimating the proportions the function fits a multivariate linear model. Ideally, the coefficients of the linear model correspond to the proportions in the admixed samples. But sometimes the coefficients take on negative values or do not sum to 1. If coefToProportion=TRUE then negative coefficients will be set to 0 and the remaining coefficients will be scaled so that they sum to 1.

Details

The methods implemented in this function were motivated by the gene expression deconvolution approach described by Abbas et al (2009), Lu et al (2003), Wang et al (2006). This approach can be used to predict the proportions of (pure) cells in a complex tissue, e.g. the proportion of blood cell types in whole blood. To define the markers, you may need to have expression data from pure populations. Then you can define markers based on a significant t-test or ANOVA across the pure populations. Next use the pure population data to estimate corresponding mean expression values. Hopefully, the array platforms and normalization methods for datE.MarkersAdmixtureTranspose and MarkerMeansPure are comparable. When dealing with Affymetrix data: we have successfully used it on untransformed MAS5 data. For statisticians: To estimate the proportions, we use the coefficients of a linear model. Specifically: datCoef= t(lm(datE.MarkersAdmixtureTranspose ~MarkerMeansPure[,-1])\$coefficients[-1,]) where datCoef is a matrix whose rows correspond to the mixed samples (rows of datE.Admixture) and the columns correspond to pure populations (e.g. cell types), i.e. the columns of MarkerMeansPure[,-1]. More details can be found in Abbas et al (2009).

Value

A list with the following components

PredictedProportions

data frame that contains the predicted proportions. The rows of PredictedProportions correspond to the admixed samples, i.e. the rows of datE.Admixture. The columns of PredictedProportions correspond to the pure populations, i.e. the columns of MarkerMeansPure[,-1].

datCoef=datCoef

data frame of numbers that is analogous to PredictedProportions. In general, datCoef will only be different from PredictedProportions if coefToProportion=TRUE. See the description of coefToProportion

conditionNumber

This is the condition number resulting from the kappa function. See the description of calculateConditionNumber.

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markersUsed

vector of character strings that contains the subset of marker names (specified in the first column of MarkerMeansPure) that match column names of datE.Admixture and that contain non-missing pure mean values.

Note

This function can be considered a wrapper of the 1m function.

Author(s)

Steve Horvath, Chaochao Cai

References

Abbas AR, Wolslegel K, Seshasayee D, Modrusan Z, Clark HF (2009) Deconvolution of Blood Microarray Data Identifies Cellular Activation Patterns in Systemic Lupus Erythematosus. PLoS ONE 4(7): e6098. doi:10.1371/journal.pone.0006098

Lu P, Nakorchevskiy A, Marcotte EM (2003) Expression deconvolution: a reinterpretation of DNA microarray data reveals dynamic changes in cell populations. Proc Natl Acad Sci U S A 100: 10370-10375.

Wang M, Master SR, Chodosh LA (2006) Computational expression deconvolution in a complex mammalian organ. BMC Bioinformatics 7: 328.

See Also

lm, kappa

propVarExplained

Proportion of variance explained by eigengenes.

Description

This function calculates the proportion of variance of genes in each module explained by the respective module eigengene.

Usage

```
propVarExplained(datExpr, colors, MEs, corFnc = "cor", corOptions = "use = 'p'")
```

Arguments

datExpr	expression data. A data frame in which columns are genes and rows ar samples. NAs are allowed and will be ignored.
colors	a vector giving module assignment for genes given in datExpr. Unique values should correspond to the names of the eigengenes in MEs.
MEs	a data frame of module eigengenes in which each column is an eigengene and each row corresponds to a sample.

corFnc character string containing the name of the function to calculate correlation.

Suggested functions include "cor" and "bicor".

corOptions further argument to the correlation function.

Details

For compatibility with other functions, entries in color are matched to a substring of names (MEs) starting at position 3. For example, the entry "turquoise" in colors will be matched to the eigengene named "MEturquoise". The first two characters of the eigengene name are ignored and can be arbitrary.

Value

A vector with one entry per eigengene containing the proportion of variance of the module explained by the eigengene.

Author(s)

Peter Langfelder

See Also

moduleEigengenes

pruneAndMergeConsensusModules

Iterative pruning and merging of (hierarchical) consensus modules

Description

This function prunes genes with low consensus eigengene-based intramodular connectivity (kME) from modules and merges modules whose consensus similarity is high. The process is repeated until the modules become stable.

Usage

```
pruneAndMergeConsensusModules(
   multiExpr,
   multiWeights = NULL,
   multiExpr.imputed = NULL,
   labels,
   unassignedLabel = if (is.numeric(labels)) 0 else "grey",
   networkOptions,
   consensusTree,

# Pruning options
   minModuleSize,
```

```
minCoreKMESize = minModuleSize/3,
minCoreKME = 0.5,
minKMEtoStay = 0.2,

# Module eigengene calculation and merging options
impute = TRUE,
trapErrors = FALSE,
calibrateMergingSimilarities = FALSE,
mergeCutHeight = 0.15,

# Behavior
iterate = TRUE,
collectGarbage = FALSE,
getDetails = TRUE,
verbose = 1, indent=0)
```

Arguments

multiExpr Expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights optional observation weights in the same format (and dimensions) as multiExpr.

These weights are used for correlation calculations with data in multiExpr.

multiExpr.imputed

If multiExpr contain missing data, this argument can be used to supply the expression data with missing data imputed. If not given, the impute.knn function

will be used to impute the missing data.

labels A vector (numeric, character or a factor) giving module labels for each variable

(gene) in multiExpr.

unassignedLabel

The label (value in labels) that represents unassigned genes. Module of this label will not enter the module eigengene clustering and will not be merged

with other modules.

networkOptions A single list of class NetworkOptions giving options for network calculation

for all of the networks, or a multiData structure containing one such list for

each input data set.

consensusTree A list of class ConsensusTree specifying the consensus calculation.

minModuleSize Minimum number of genes in a module. Modules that have fewer genes (after

trimming) will be removed (i.e., their genes will be given the unassigned label).

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize

genes with consensus eigengene connectivity at least minCoreKME, the module

is disbanded (its genes are unlabeled).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose consensus eigengene connectivity to their module eigengene is

lower than minKMEtoStay are removed from the module.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

calibrateMergingSimilarities

Logical: should module eigengene similarities be calibrated before calculating the consensus? Although calibration is in principle desirable, the calibration methods currently available assume large data and do not work very well on

eigengene similarities.

mergeCutHeight Dendrogram cut height for module merging.

iterate Logical: should the pruning and merging process be iterated until no changes

occur? If FALSE, only one iteration will be carried out.

collectGarbage Logical: should garbage be collected after some of the memory-intensive steps?

getDetails Logical: should certain intermediate results be returned? These include labels

and module merging information at each iteration (see return value).

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Value

If input getDetails is FALSE, a vector the resulting module labels. If getDetails is TRUE, a list with these components:

labels The resulting module labels

details A list. The first component, named originalLabels, contains a copy of the in-

put labels. The following components are named Iteration.1, Iteration.2 etc and contain, for each iteration, components prunedLabels (the result of

pruning in that iteration) and mergeInfo (result of the call to hierarchicalMergeCloseModules

in that iteration).

Author(s)

Peter Langfelder

See Also

The underlying functions pruneConsensusModules and hierarchicalMergeCloseModules.

pruneConsensusModules Prune (hierarchical) consensus modules by removing genes with low eigengene-based intramodular connectivity

Description

This function prunes (hierarchical) consensus modules by removing genes with low eigengene-based intramodular connectivity (KME) and by removing modules that do not have a certain minimum number of genes with a required minimum KME.

Usage

```
pruneConsensusModules( multiExpr,
 multiWeights = NULL,
 multiExpr.imputed = NULL,
 MEs = NULL,
  labels,
  unassignedLabel = if (is.numeric(labels)) 0 else "grey",
  networkOptions,
  consensusTree,
 minModuleSize,
 minCoreKMESize = minModuleSize/3,
 minCoreKME = 0.5,
 minKMEtoStay = 0.2,
  # Module eigengene calculation options
  impute = TRUE,
  collectGarbage = FALSE,
  checkWeights = TRUE,
  verbose = 1, indent=0)
```

Arguments

multiExpr

Expression data in the multi-set format (see checkSets). A vector of lists, one per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights

optional observation weights in the same format (and dimensions) as multiExpr. These weights are used for correlation calculations with data in multiExpr.

multiExpr.imputed

If multiExpr contain missing data, this argument can be used to supply the expression data with missing data imputed. If not given, the impute.knn function will be used to impute the missing data.

MEs Optional consensus module eigengenes, in multi-set format analogous to that of

multiExpr.

labels A vector (numeric, character or a factor) giving module labels for each variable

(gene) in multiExpr.

unassignedLabel

The label (value in labels) that represents unassigned genes. Module of this label will not enter the module eigengene clustering and will not be merged

with other modules.

networkOptions A single list of class NetworkOptions giving options for network calculation

for all of the networks, or a multiData structure containing one such list for

each input data set.

consensusTree A list of class ConsensusTree specifying the consensus calculation.

minModuleSize Minimum number of genes in a module. Modules that have fewer genes (after

trimming) will be removed (i.e., their genes will be given the unassigned label).

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize

genes with consensus eigengene connectivity at least minCoreKME, the module

is disbanded (its genes are unlabeled).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose consensus eigengene connectivity to their module eigengene is

lower than minKMEtoStay are removed from the module.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

collectGarbage Logical: should garbage be collected after some of the memory-intensive steps?

checkWeights Logical: should multiWeights be checked to make sure their dimensions are

concordant with multiExpr and the weights are valid?

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Value

The pruned module labels: a vector of the same form as the input labels.

Author(s)

Peter Langfelder

334 qvalue

PWLists	Pathways with Corresponding Gene Markers - Compiled by Mike
	Palazzolo and Jim Wang from CHDI

Description

This matrix gives a predefined set of marker genes for many immune response pathways, as assembled by Mike Palazzolo and Jim Wang from CHDI, and colleagues. It is used with userListEnrichment to search user-defined gene lists for enrichment.

Usage

```
data(PWLists)
```

Format

A 124350 x 2 matrix of characters containing 2724 Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <gene set>__<reference>.

Source

For more information about this list, please see userListEnrichment

Examples

```
data(PWLists)
head(PWLists)
```

qvalue

Estimate the q-values for a given set of p-values

Description

Estimate the q-values for a given set of p-values. The q-value of a test measures the proportion of false positives incurred (called the false discovery rate) when that particular test is called significant.

Usage

```
qvalue(p, lambda=seq(0,0.90,0.05), pi0.method="smoother", fdr.level=NULL, robust=FALSE,
    smooth.df=3, smooth.log.pi0=FALSE)
```

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Arguments

A vector of p-values (only necessary input) р lambda The value of the tuning parameter to estimate π_0 . Must be in [0,1). Optional, see Storey (2002). pi0.method Either "smoother" or "bootstrap"; the method for automatically choosing tuning parameter in the estimation of π_0 , the proportion of true null hypotheses fdr.level A level at which to control the FDR. Must be in (0,1]. Optional; if this is selected, a vector of TRUE and FALSE is returned that specifies whether each q-value is less than fdr.level or not. An indicator of whether it is desired to make the estimate more robust for small robust p-values and a direct finite sample estimate of pFDR. Optional. Number of degrees-of-freedom to use when estimating π_0 with a smoother. Opsmooth.df tional. smooth.log.pi0 If TRUE and pi0.method = "smoother", π_0 will be estimated by applying a smoother to a scatterplot of $log \pi_0$ estimates against the tuning parameter λ .

Details

If no options are selected, then the method used to estimate π_0 is the smoother method described in Storey and Tibshirani (2003). The bootstrap method is described in Storey, Taylor & Siegmund (2004).

Value

A list containing:

call function call

pi0 an estimate of the proportion of null p-values

qvalues a vector of the estimated q-values (the main quantity of interest)

pvalues a vector of the original p-values

Optional.

significant if fdr.level is specified, and indicator of whether the q-value fell below fdr.level

(taking all such q-values to be significant controls FDR at level fdr.level)

Note

This function is adapted from package qvalue. The reason we provide our own copy is that package qvalue contains additional functionality that relies on Tcl/Tk which has led to multiple problems. Our copy does not require Tcl/Tk.

Author(s)

John D. Storey <jstorey@u.washington.edu>, adapted for WGCNA by Peter Langfelder

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References

Storey JD. (2002) A direct approach to false discovery rates. Journal of the Royal Statistical Society, Series B, 64: 479-498.

Storey JD and Tibshirani R. (2003) Statistical significance for genome-wide experiments. Proceedings of the National Academy of Sciences, 100: 9440-9445.

Storey JD. (2003) The positive false discovery rate: A Bayesian interpretation and the q-value. Annals of Statistics, 31: 2013-2035.

Storey JD, Taylor JE, and Siegmund D. (2004) Strong control, conservative point estimation, and simultaneous conservative consistency of false discovery rates: A unified approach. Journal of the Royal Statistical Society, Series B, 66: 187-205.

qvalue.restricted

qvalue convenience wrapper

Description

This function calls qvalue on finite input p-values, optionally traps errors from the q-value calculation, and returns just the q values.

Usage

```
qvalue.restricted(p, trapErrors = TRUE, ...)
```

Arguments

p a vector of p-values. Missing data are allowed and will be removed.

trapErrors logical: should errors generated by function qvalue trapped? If TRUE, the errors

will be silently ignored and the returned q-values will all be NA.

... other arguments to function qvalue.

Value

A vector of q-values. Entries whose corresponding p-values were not finite will be NA.

Author(s)

Peter Langfelder

See Also

qvalue

randIndex 337

rand	١h	nd	eχ

Rand index of two partitions

Description

Computes the Rand index, a measure of the similarity between two clusterings.

Usage

```
randIndex(tab, adjust = TRUE)
```

Arguments

tab a matrix giving the cross-tabulation table of two clusterings.

adjust logical: should the "adjusted" version be computed?

Value

the Rand index of the input table.

Author(s)

Steve Horvath

References

W. M. Rand (1971). "Objective criteria for the evaluation of clustering methods". Journal of the American Statistical Association 66: 846-850

rankPvalue

Estimate the p-value for ranking consistently high (or low) on multiple lists

Description

The function rankPvalue calculates the p-value for observing that an object (corresponding to a row of the input data frame datS) has a consistently high ranking (or low ranking) according to multiple ordinal scores (corresponding to the columns of the input data frame datS).

Usage

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Arguments

datS a data frame whose rows represent objects that will be ranked. Each column

of datS represents an ordinal variable (which can take on negative values). The columns correspond to (possibly signed) object significance measures, e.g.,

statistics (such as Z statistics), ranks, or correlations.

columnweights allows the user to input a vector of non-negative numbers reflecting weights for

the different columns of datZ. If it is set to NULL then all weights are equal.

na.last controls the treatment of missing values (NAs) in the rank function. If TRUE,

missing values in the data are put last (i.e. they get the highest rank values). If FALSE, they are put first; if NA, they are removed; if "keep" they are kept with

rank NA. See rank for more details.

ties.method represents the ties method used in the rank function for the percentile rank

method. See rank for more details.

calculateQvalue

logical: should q-values be calculated? If set to TRUE then the function calculates corresponding q-values (local false discovery rates) using the qvalue package, see Storey JD and Tibshirani R. (2003). This option assumes that qvalue

package has been installed.

pValueMethod determines which method is used for calculating p-values. By default it is set to

"all", i.e. both methods are used. If it is set to "rank" then only the percentile rank method is used. If it set to "scale" then only the scale method will be used.

Details

The function calculates asymptotic p-values (and optionally q-values) for testing the null hypothesis that the values in the columns of datS are independent. This allows us to find objects (rows) with consistently high (or low) values across the columns.

Example: Imagine you have 5 vectors of Z statistics corresponding to the columns of datS. Further assume that a gene has ranks 1,1,1,1,20 in the 5 lists. It seems very significant that the gene ranks number 1 in 4 out of the 5 lists. The function rankPvalue can be used to calculate a p-value for this occurrence.

The function uses the central limit theorem to calculate asymptotic p-values for two types of test statistics that measure consistently high or low ordinal values. The first method (referred to as percentile rank method) leads to accurate estimates of p-values if datS has at least 4 columns but it can be overly conservative. The percentile rank method replaces each column datS by the ranked version rank(datS[,i]) (referred to ask low ranking) and by rank(-datS[,i]) (referred to as high ranking). Low ranking and high ranking allow one to find consistently small values or consistently large values of datS, respectively. All ranks are divided by the maximum rank so that the result lies in the unit interval [0,1]. In the following, we refer to rank/max(rank) as percentile rank. For a given object (corresponding to a row of datS) the observed percentile rank follows approximately a uniform distribution under the null hypothesis. The test statistic is defined as the sum of the percentile ranks (across the columns of datS). Under the null hypothesis that there is no relationship between the rankings of the columns of datS, this (row sum) test statistic follows a distribution that is given by the convolution of random uniform distributions. Under the null hypothesis, the individual percentile ranks are independent and one can invoke the central limit theorem to argue that the row sum test statistic follows asymptotically a normal distribution. It is well-known that the speed of

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convergence to the normal distribution is extremely fast in case of identically distributed uniform distributions. Even when datS has only 4 columns, the difference between the normal approximation and the exact distribution is negligible in practice (Killmann et al 2001). In summary, we use the central limit theorem to argue that the sum of the percentile ranks follows a normal distribution whose mean and variance can be calculated using the fact that the mean value of a uniform random variable (on the unit interval) equals 0.5 and its variance equals 1/12.

The second method for calculating p-values is referred to as scale method. It is often more powerful but its asymptotic p-value can only be trusted if either datS has a lot of columns or if the ordinal scores (columns of datS) follow an approximate normal distribution. The scale method scales (or standardizes) each ordinal variable (column of datS) so that it has mean 0 and variance 1. Under the null hypothesis of independence, the row sum follows approximately a normal distribution if the assumptions of the central limit theorem are met. In practice, we find that the second approach is often more powerful but it makes more distributional assumptions (if datS has few columns).

Value

A list whose actual content depends on which p-value methods is selected, and whether q0values are calculated. The following inner components are calculated, organized in outer components datoutrank and datoutscale,:

pValueExtremeRank

This is the minimum between pValueLowRank and pValueHighRank, i.e. min(pValueLow, pValueHigh)

pValueLowRank Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

pValueHighRank Asymptotic p-value for observing a consistently low value across the columns of datS based on the rank method.

pValueExtremeScale

This is the minimum between pValueLowScale and pValueHighScale, i.e. min(pValueLow, pValueHigh)

pValueLowScale Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method.

pValueHighScale

Asymptotic p-value for observing a consistently low value across the columns of datS based on the Scale method.

qValueExtremeRank

local false discovery rate (q-value) corresponding to the p-value pValueExtremeR-ank

qValueLowRank local false discovery rate (q-value) corresponding to the p-value pValueLowRank qValueHighRank local false discovery rate (q-value) corresponding to the p-value pValueHighRank

qValueExtremeScale

local false discovery rate (q-value) corresponding to the p-value pValueExtremeScale

qValueLowScale local false discovery rate (q-value) corresponding to the p-value pValueLowS-

qValueHighScale

local false discovery rate (q-value) corresponding to the p-value pValueHigh-Scale

Author(s)

Steve Horvath

References

Killmann F, VonCollani E (2001) A Note on the Convolution of the Uniform and Related Distributions and Their Use in Quality Control. Economic Quality Control Vol 16 (2001), No. 1, 17-41.ISSN 0940-5151

Storey JD and Tibshirani R. (2003) Statistical significance for genome-wide experiments. Proceedings of the National Academy of Sciences, 100: 9440-9445.

See Also

rank, qvalue

recutBlockwiseTrees

Repeat blockwise module detection from pre-calculated data

Description

Given consensus networks constructed for example using blockwiseModules, this function (re-)detects modules in them by branch cutting of the corresponding dendrograms. If repeated branch cuts of the same gene network dendrograms are desired, this function can save substantial time by re-using already calculated networks and dendrograms.

Usage

```
recutBlockwiseTrees(
 datExpr,
  goodSamples, goodGenes,
 blocks,
 TOMFiles,
 dendrograms,
  corType = "pearson",
  networkType = "unsigned",
 deepSplit = 2,
  detectCutHeight = 0.995, minModuleSize = min(20, ncol(datExpr)/2 ),
 maxCoreScatter = NULL, minGap = NULL,
 maxAbsCoreScatter = NULL, minAbsGap = NULL,
 minSplitHeight = NULL, minAbsSplitHeight = NULL,
  useBranchEigennodeDissim = FALSE,
 minBranchEigennodeDissim = mergeCutHeight,
  pamStage = TRUE, pamRespectsDendro = TRUE,
 minCoreKME = 0.5, minCoreKMESize = minModuleSize/3,
```

```
minKMEtoStay = 0.3,
reassignThreshold = 1e-6,
mergeCutHeight = 0.15, impute = TRUE,
trapErrors = FALSE, numericLabels = FALSE,
verbose = 0, indent = 0,
...)
```

Arguments

datExpr expression data. A data frame in which columns are genes and rows ar samples.

NAs are allowed, but not too many.

goodSamples a logical vector specifying which samples are considered "good" for the analy-

sis. See goodSamplesGenes.

goodGenes a logical vector with length equal number of genes in multiExpr that specifies

which genes are considered "good" for the analysis. See goodSamplesGenes.

blocks specification of blocks in which hierarchical clustering and module detection

should be performed. A numeric vector with one entry per gene of $\mathtt{multiExpr}$

giving the number of the block to which the corresponding gene belongs.

TOMFiles a vector of character strings specifying file names in which the block-wise topo-

logical overlaps are saved.

dendrograms a list of length equal the number of blocks, in which each component is a hier-

archical clustering dendrograms of the genes that belong to the block.

corType character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pariwise.complete.obs

option.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

deepSplit integer value between 0 and 4. Provides a simplified control over how sensitive

module detection should be to module splitting, with 0 least and 4 most sensitive.

See cutreeDynamic for more details.

detectCutHeight

dendrogram cut height for module detection. See cutreeDynamic for more de-

tails.

minModuleSize minimum module size for module detection. See cutreeDynamic for more de-

ails.

maxCoreScatter maximum scatter of the core for a branch to be a cluster, given as the fraction of

cutHeight relative to the 5th percentile of joining heights. See cutreeDynamic

for more details.

minGap minimum cluster gap given as the fraction of the difference between cutHeight

and the 5th percentile of joining heights. See cutreeDynamic for more details.

maxAbsCoreScatter

maximum scatter of the core for a branch to be a cluster given as absolute heights. If given, overrides maxCoreScatter. See cutreeDynamic for more

details.

minAbsGap minimum cluster gap given as absolute height difference. If given, overrides

minGap. See cutreeDynamic for more details.

minSplitHeight Minimum split height given as the fraction of the difference between cutHeight

and the 5th percentile of joining heights. Branches merging below this height will automatically be merged. Defaults to zero but is used only if minAbsSplitHeight

below is NULL.

minAbsSplitHeight

Minimum split height given as an absolute height. Branches merging below this height will automatically be merged. If not given (default), will be determined

 $from \ {\tt minSplitHeight} \ above.$

useBranchEigennodeDissim

Logical: should branch eigennode (eigengene) dissimilarity be considered when

merging branches in Dynamic Tree Cut?

minBranchEigennodeDissim

Minimum consensus branch eigennode (eigengene) dissimilarity for branches to be considerd separate. The branch eigennode dissimilarity in individual sets is simly 1-correlation of the eigennodes; the consensus is defined as quantile with

 $probability\ {\tt consensusQuantile}.$

pamStage logical. If TRUE, the second (PAM-like) stage of module detection will be

performed. See cutreeDynamic for more details.

pamRespectsDendro

Logical, only used when pamStage is TRUE. If TRUE, the PAM stage will respect the dendrogram in the sense an object can be PAM-assigned only to clusters that lie below it on the branch that the object is merged into. See cutreeDynamic

for more details.

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize

genes with eigengene connectivity at least minCoreKME, the module is disbanded (its genes are unlabeled and returned to the pool of genes waiting for mofule de-

tection).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose eigengene connectivity to their module eigengene is lower than

minKMEtoStay are removed from the module.

reassignThreshold

p-value ratio threshold for reassigning genes between modules. See Details.

mergeCutHeight dendrogram cut height for module merging.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

numericLabels logical: should the returned modules be labeled by colors (FALSE), or by num-

bers (TRUE)?

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

... Other arguments.

Details

For details on blockwise module detection, see blockwiseModules. This function implements the module detection subset of the functionality of blockwiseModules; network construction and clustering must be performed in advance. The primary use of this function is to experiment with module detection settings without having to re-execute long network and clustering calculations whose results are not affected by the cutting parameters.

This function takes as input the networks and dendrograms that are produced by blockwiseModules. Working block by block, modules are identified in the dendrogram by the Dynamic Hybrid Tree Cut algorithm. Found modules are trimmed of genes whose correlation with module eigengene (KME) is less than minKMEtoStay. Modules in which fewer than minCoreKMESize genes have KME higher than minCoreKME are disbanded, i.e., their constituent genes are pronounced unassigned.

After all blocks have been processed, the function checks whether there are genes whose KME in the module they assigned is lower than KME to another module. If p-values of the higher correlations are smaller than those of the native module by the factor reassignThresholdPS, the gene is reassigned to the closer module.

In the last step, modules whose eigengenes are highly correlated are merged. This is achieved by clustering module eigengenes using the dissimilarity given by one minus their correlation, cutting the dendrogram at the height mergeCutHeight and merging all modules on each branch. The process is iterated until no modules are merged. See mergeCloseModules for more details on module merging.

Value

A list with the following components:

colors a vector of color or numeric module labels for all genes.

unmergedColors a vector of color or numeric module labels for all genes before module merging.

MEs a data frame containing module eigengenes of the found modules (given by

colors).

MESOK logical indicating whether the module eigengenes were calculated without er-

rors.

Author(s)

Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

blockwiseModules for full module calculation; cutreeDynamic for adaptive branch cutting in hierarchical clustering dendrograms; mergeCloseModules for merging of close modules.

recutConsensusTrees Repeat blockwise consensus module detection from pre-calculated data

Description

Given consensus networks constructed for example using blockwiseConsensusModules, this function (re-)detects modules in them by branch cutting of the corresponding dendrograms. If repeated branch cuts of the same gene network dendrograms are desired, this function can save substantial time by re-using already calculated networks and dendrograms.

Usage

```
recutConsensusTrees(
 multiExpr,
  goodSamples, goodGenes,
  blocks,
  TOMFiles,
  dendrograms,
  corType = "pearson",
  networkType = "unsigned",
  deepSplit = 2,
  detectCutHeight = 0.995, minModuleSize = 20,
  checkMinModuleSize = TRUE,
 maxCoreScatter = NULL, minGap = NULL,
 maxAbsCoreScatter = NULL, minAbsGap = NULL,
 minSplitHeight = NULL, minAbsSplitHeight = NULL,
  useBranchEigennodeDissim = FALSE,
 minBranchEigennodeDissim = mergeCutHeight,
  pamStage = TRUE, pamRespectsDendro = TRUE,
  trimmingConsensusQuantile = 0,
 minCoreKME = 0.5, minCoreKMESize = minModuleSize/3,
 minKMEtoStay = 0.2,
  reassignThresholdPS = 1e-4,
 mergeCutHeight = 0.15,
 mergeConsensusQuantile = trimmingConsensusQuantile,
  impute = TRUE,
  trapErrors = FALSE,
  numericLabels = FALSE,
```

verbose = 2, indent = 0)

Arguments

multiExpr expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression

data, with rows corresponding to samples and columns to genes or probes.

goodSamples a list with one component per set. Each component is a logical vector specifying

which samples are considered "good" for the analysis. See goodSamplesGenesMS.

goodGenes a logical vector with length equal number of genes in multiExpr that specifies

which genes are considered "good" for the analysis. See goodSamplesGenesMS.

blocks specification of blocks in which hierarchical clustering and module detection

should be performed. A numeric vector with one entry per gene of multiExpr giving the number of the block to which the corresponding gene belongs.

TOMFiles a vector of character strings specifying file names in which the block-wise topo-

logical overlaps are saved.

dendrograms a list of length equal the number of blocks, in which each component is a hier-

archical clustering dendrograms of the genes that belong to the block.

corType character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pariwise.complete.obs

option.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency. Note that while no new networks are computed in this function, this parameter affects the interpretation of correlations in

this function.

deepSplit integer value between 0 and 4. Provides a simplified control over how sensitive

module detection should be to module splitting, with 0 least and 4 most sensitive.

See cutreeDynamic for more details.

detectCutHeight

dendrogram cut height for module detection. See cutreeDynamic for more de-

tails.

minModuleSize minimum module size for module detection. See cutreeDynamic for more de-

tans

checkMinModuleSize

logical: should sanity checks be performed on minModuleSize?

maxCoreScatter maximum scatter of the core for a branch to be a cluster, given as the fraction of

cutHeight relative to the 5th percentile of joining heights. See cutreeDynamic

for more details.

minGap minimum cluster gap given as the fraction of the difference between cutHeight

and the 5th percentile of joining heights. See cutreeDynamic for more details.

maxAbsCoreScatter

maximum scatter of the core for a branch to be a cluster given as absolute heights. If given, overrides maxCoreScatter. See cutreeDynamic for more

details.

minAbsGap minimum cluster gap given as absolute height difference. If given, overrides

minGap. See cutreeDynamic for more details.

minSplitHeight Minimum split height given as the fraction of the difference between cutHeight and the 5th percentile of joining heights. Branches merging below this height will automatically be merged. Defaults to zero but is used only if minAbsSplitHeight

below is NULL.

minAbsSplitHeight

Minimum split height given as an absolute height. Branches merging below this height will automatically be merged. If not given (default), will be determined from minSplitHeight above.

useBranchEigennodeDissim

Logical: should branch eigennode (eigengene) dissimilarity be considered when merging branches in Dynamic Tree Cut?

minBranchEigennodeDissim

Minimum consensus branch eigennode (eigengene) dissimilarity for branches to be considered separate. The branch eigennode dissimilarity in individual sets is simly 1-correlation of the eigennodes; the consensus is defined as quantile with probability consensusQuantile.

pamStage logical. If TRUE, the second (PAM-like) stage of module detection will be performed. See cutreeDynamic for more details.

pamRespectsDendro

Logical, only used when pamStage is TRUE. If TRUE, the PAM stage will respect the dendrogram in the sense an object can be PAM-assigned only to clusters that lie below it on the branch that the object is merged into. See cutreeDynamic for more details.

trimmingConsensusQuantile

a number between 0 and 1 specifying the consensus quantile used for kME calculation that determines module trimming according to the arguments below.

minCoreKME a number between 0 and 1. If a detected module does not have at least minModuleKMESize genes with eigengene connectivity at least minCoreKME, the module is disbanded

(its genes are unlabeled and returned to the pool of genes waiting for mofule de-

tection).

minCoreKMESize see minCoreKME above.

minKMEtoStay genes whose eigengene connectivity to their module eigengene is lower than

minKMEtoStay are removed from the module.

reassignThresholdPS

per-set p-value ratio threshold for reassigning genes between modules. See De-

tails.

mergeCutHeight dendrogram cut height for module merging.

mergeConsensusQuantile

consensus quantile for module merging. See mergeCloseModules for details.

impute logical: should imputation be used for module eigengene calculation? See

moduleEigengenes for more details.

trapErrors logical: should errors in calculations be trapped?

numericLabels logical: should the returned modules be labeled by colors (FALSE), or by num-

bers (TRUE)?

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

For details on blockwise consensus module detection, see blockwiseConsensusModules. This function implements the module detection subset of the functionality of blockwiseConsensusModules; network construction and clustering must be performed in advance. The primary use of this function is to experiment with module detection settings without having to re-execute long network and clustering calculations whose results are not affected by the cutting parameters.

This function takes as input the networks and dendrograms that are produced by blockwiseConsensusModules. Working block by block, modules are identified in the dendrograms by the Dynamic Hybrid tree cut. Found modules are trimmed of genes whose consensus module membership kME (that is, correlation with module eigengene) is less than minKMEtoStay. Modules in which fewer than minCoreKMESize genes have consensus KME higher than minCoreKME are disbanded, i.e., their constituent genes are pronounced unassigned.

After all blocks have been processed, the function checks whether there are genes whose KME in the module they assigned is lower than KME to another module. If p-values of the higher correlations are smaller than those of the native module by the factor reassignThresholdPS (in every set), the gene is re-assigned to the closer module.

In the last step, modules whose eigengenes are highly correlated are merged. This is achieved by clustering module eigengenes using the dissimilarity given by one minus their correlation, cutting the dendrogram at the height mergeCutHeight and merging all modules on each branch. The process is iterated until no modules are merged. See mergeCloseModules for more details on module merging.

Value

A list with the following components:

colors module assignment of all input genes. A vector containing either character

strings with module colors (if input numericLabels was unset) or numeric module labels (if numericLabels was set to TRUE). The color "grey" and the numeric

label 0 are reserved for unassigned genes.

unmergedColors module colors or numeric labels before the module merging step.

multiMEs module eigengenes corresponding to the modules returned in colors, in multi-

set format. A vector of lists, one per set, containing eigengenes, proportion of variance explained and other information. See multiSetMEs for a detailed

description.

Note

Basic sanity checks are performed on given arguments, but it is left to the user's responsibility to provide valid input.

348 redWhiteGreen

Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

blockwiseConsensusModules for the full blockwise modules calculation. Parts of its output are natural input for this function.

cutreeDynamic for adaptive branch cutting in hierarchical clustering dendrograms; mergeCloseModules for merging of close modules.

redWhiteGreen

Red-white-green color sequence

Description

Generate a red-white-green color sequence of a given length.

Usage

```
redWhiteGreen(n, gamma = 1)
```

Arguments

n number of colors to be returned

gamma color correction power

Details

The function returns a color vector that starts with pure green, gradually turns into white and then to red. The power gamma can be used to control the behaviour of the quarter- and three quarter-values (between red and white, and white and green, respectively). Higher powers will make the mid-colors more white, while lower powers will make the colors more saturated, respectively.

Value

A vector of colors of length n.

Author(s)

Peter Langfelder

Examples

```
par(mfrow = c(3, 1))
displayColors(redWhiteGreen(50));
displayColors(redWhiteGreen(50, 3));
displayColors(redWhiteGreen(50, 0.5));
```

relative CorPrediction Success

Compare prediction success

Description

Compare prediction success of several gene screening methods.

Usage

```
relativeCorPredictionSuccess(
  corPredictionNew,
  corPredictionStandard,
  corTestSet,
  topNumber = 100)
```

Arguments

corPredictionNew

Matrix of predictor statistics

corPredictionStandard

Reference presdictor statistics

corTestSet Correlations of predictor variables with trait in test set topNumber A vector giving the numbers of top genes to consider

Value

Data frame with components

topNumber copy of the input topNumber kruskalp Kruskal-Wallis p-values

Author(s)

Steve Horvath

See Also

corPredictionSuccess

removeGreyME

Removes the grey eigengene from a given collection of eigengenes.

Description

Given module eigengenes either in a single data frame or in a multi-set format, removes the grey eigengenes from each set. If the grey eigengenes are not found, a warning is issued.

Usage

```
removeGreyME(MEs, greyMEName = paste(moduleColor.getMEprefix(), "grey", sep=""))
```

Arguments

MEs Module eigengenes, either in a single data frame (typicaly for a single set), or in

a multi-set format. See checkSets for a description of the multi-set format.

greyMEName Name of the module eigengene (in each corresponding data frame) that corre-

sponds to the grey color. This will typically be "PCgrey" or "MEgrey". If the module eigengenes were calculated using standard functions in this library, the

default should work.

Value

Module eigengenes in the same format as input (either a single data frame or a vector of lists) with the grey eigengene removed.

Author(s)

Peter Langfelder, <Peter.Langfelder@gmail.com>

removePrincipalComponents

Remove leading principal components from data

Description

This function calculates a fixed number of the first principal components of the given data and returns the residuals of a linear regression of each column on the principal components.

Usage

removePrincipalComponents(x, n)

replaceMissing 351

Arguments

x Input data, a numeric matrix. All entries must be non-missing and finite.

n Number of principal components to remove. This must be smaller than the

smaller of the number of rows and columns in x.

Value

A matrix of residuals of the same dimensions as x.

Author(s)

Peter Langfelder

See Also

svd for singular value decomposition, 1m for linear regression

replaceMissing

Replace missing values with a constant.

Description

A convenience function for replacing missing values with a (non-missing) constant.

Usage

```
replaceMissing(x, replaceWith)
```

Arguments

x An atomic vector or array.

replaceWith Value to replace missing entries in x. The default is FALSE for logical vectors, 0

for numeric vectors, and empty string "" for character vectors.

Value

x with missing data replaced.

Author(s)

Peter Langfelder

352 returnGeneSetsAsList

Examples

```
logVec = c(TRUE, FALSE, NA, TRUE);
replaceMissing(logVec)

numVec = c(1,2,3,4,NA,2)
replaceMissing(numVec)
```

returnGeneSetsAsList Return pre-defined gene lists in several biomedical categories.

Description

This function returns gene sets for use with other R functions. These gene sets can include inputted lists of genes and files containing user-defined lists of genes, as well as a pre-made collection of brain, blood, and other biological lists. The function returns gene lists associated with each category for use with other enrichment strategies (i.e., GSVA).

Usage

```
returnGeneSetsAsList(
   fnIn = NULL, catNmIn = fnIn,
   useBrainLists = FALSE, useBloodAtlases = FALSE,
   useStemCellLists = FALSE, useBrainRegionMarkers = FALSE,
   useImmunePathwayLists = FALSE, geneSubset=NULL)
```

Arguments

fnIn A vector of file names containing user-defined lists. These files must be in one

of three specific formats (see details section). The default (NULL) may only be

used if one of the "use____" parameters is TRUE.

catNmIn A vector of category names corresponding to each fnIn. This name will be

appended to each overlap corresponding to that filename. The default sets the

category names as the corresponding file names.

useBrainLists If TRUE, a pre-made set of brain-derived enrichment lists will be added to any

user-defined lists for enrichment comparison. The default is FALSE. See refer-

ences section for related references.

useBloodAtlases

If TRUE, a pre-made set of blood-derived enrichment lists will be added to any user-defined lists for enrichment comparison. The default is FALSE. See

references section for related references.

useStemCellLists

If TRUE, a pre-made set of stem cell (SC)-derived enrichment lists will be added to any user-defined lists for enrichment comparison. The default is FALSE. See references section for related references.

returnGeneSetsAsList 353

useBrainRegionMarkers

If TRUE, a pre-made set of enrichment lists for human brain regions will be added to any user-defined lists for enrichment comparison. The default is FALSE. These lists are derived from data from the Allen Human Brain Atlas (https://human.brain-map.org/). See references section for more details.

useImmunePathwayLists

If TRUE, a pre-made set of enrichment lists for immune system pathways will be added to any user-defined lists for enrichment comparison. The default is FALSE. These lists are derived from the lab of Daniel R Saloman. See references section for more details.

geneSubset

A vector of gene (or other) identifiers. If entered, only genes in this list will be returned in the output, otherwise all genes in each category will be returned (default, geneSubset=NULL).

Details

User-inputted files for fnIn can be in one of three formats:

- 1) Text files (must end in ".txt") with one list per file, where the first line is the list descriptor and the remaining lines are gene names corresponding to that list, with one gene per line. For example Ribosome RPS4 RPS8 ...
- 2) Gene / category files (must be csv files), where the first line is the column headers corresponding to Genes and Lists, and the remaining lines correspond to the genes in each list, for any number of genes and lists. For example: Gene, Category RPS4, Ribosome RPS8, Ribosome ... NDUF1, Mitohcondria NDUF3, Mitochondria ... MAPT, AlzheimersDisease PSEN1, AlzheimersDisease PSEN2, AlzheimersDisease ...
- 3) Module membership (kME) table in csv format. Currently, the module assignment is the only thing that is used, so as long as the Gene column is 2nd and the Module column is 3rd, it doesn't matter what is in the other columns. For example, PSID, Gene, Module, <other columns> <psid>, RPS4, blue, <other columns> <psid>, NDUF1, red, <other columns> <psid>, RPS8, blue, <other columns> <psid>, NDUF3, red, <other columns> <psid>, MAPT, green, <other columns> ...

Value

geneSets

A list of categories in alphabetical order, where each compnent of the list is a character vector of all genes corresponding to the named category. For example: geneSets = list(category1=c("gene1","gene2"),category2=c("gene3","gene4","gene5"))

Author(s)

Jeremy Miller

References

Please see the help file for userListEnrichment in the WGCNA library for references for the predefined lists. 354 rgcolors.func

Examples

```
# Example: Return a list of genes for various immune pathways
geneSets = returnGeneSetsAsList(useImmunePathwayLists=TRUE)
geneSets[7:8]
```

rgcolors.func

Red and Green Color Specification

Description

This function creates a vector of n "contiguous" colors, corresponding to n intensities (between 0 and 1) of the red, green and blue primaries, with the blue intensities set to zero. The values returned by rgcolors. func can be used with a col= specification in graphics functions or in par.

Usage

```
rgcolors.func(n=50)
```

Arguments

n

the number of colors (≥ 1) to be used in the red and green palette.

Value

a character vector of color names. Colors are specified directly in terms of their RGB components with a string of the form "#RRGGBB", where each of the pairs RR, GG, BB consist of two hexadecimal digits giving a value in the range 00 to FF.

Author(s)

```
Sandrine Dudoit, <sandrine@stat.berkeley.edu>
Jane Fridlyand, <janef@stat.berkeley.edu>
```

See Also

```
plotCor, plotMat, colors, rgb, image.
```

Examples

```
rgcolors.func(n=5)
```

```
sampledBlockwiseModules
```

Blockwise module identification in sampled data

Description

This function repeatedly resamples the samples (rows) in supplied data and identifies modules on the resampled data.

Usage

```
sampledBlockwiseModules(
 datExpr,
  nRuns,
  startRunIndex = 1,
  endRunIndex = startRunIndex + nRuns - skipUnsampledCalculation,
  replace = FALSE,
  fraction = if (replace) 1.0 else 0.63,
  randomSeed = 12345,
  checkSoftPower = TRUE,
  nPowerCheckSamples = 2000,
  skipUnsampledCalculation = FALSE,
  corType = "pearson",
 power = 6,
  networkType = "unsigned",
  saveTOMs = FALSE,
  saveTOMFileBase = "TOM",
 verbose = 2, indent = 0)
```

Arguments

datExpr	Expression data. A matrix (preferred) or data frame in which columns are genes and rows ar samples.
nRuns	Number of sampled network construction and module identification runs. If skipUnsampledCalculation is FALSE, one extra calculation (the first) will contain the unsampled calculation.
startRunIndex	Number to be assigned to the start run. The run number or index is used to make saved files unique. It is also used in setting the seed for each run to allow the runs to be replicated in smaller or larger batches.
endRunIndex	Number (index) of the last run. If given, nRuns is ignored.
replace	Logical: should samples (observations or rows in entries in multiExpr) be sampled with replacement?
fraction	Fraction of samples to sample for each run.

randomSeed Integer specifying the random seed. If non-NULL, the random number genera-

tor state is saved before the seed is set and restored at the end of the function. If NULL, the random number generator state is not saved nor changed at the start,

and not restored at the end.

checkSoftPower Logical: should the soft-tresholding power be adjusted to approximately match

the connectivity distribution of the sampled data set and the full data set?

nPowerCheckSamples

Number of genes to be sampled from the full data set to calculate connectivity

and match soft-tresholding powers.

skipUnsampledCalculation

Logical: should a calculation on original (not resampled) data be skipped?

corType Character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pairwise.complete.obs

option.

power Soft-thresholding power for network construction.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

saveTOMs Logical: should the networks (topological overlaps) be saved for each run? Note

that for large data sets (tens of thousands of nodes) the TOM files are rather

large.

saveTOMFileBase

Character string giving the base of the file names for TOMs. The actual file

names will consist of a concatenation of saveTOMFileBase and "-run-<run

number>-Block-<block number>.RData".

... Other arguments to blockwiseModules.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

For each run, samples (but not genes) are randomly sampled to obtain a perturbed data set; a full network analysis and module identification is carried out, and the results are returned in a list with one component per run.

For each run, the soft-thresholding power can optionally be adjusted such that the mean adjacency in the re-sampled data set equals the mean adjacency in the original data.

Value

A list with one component per run. Each component is a list with the following components:

mods The output of the function blockwiseModules applied to a resampled data set.

samples Indices of the samples selected for the resampled data step for this run.

powers Actual soft-thresholding powers used in this run.

Author(s)

Peter Langfelder

References

An application of this function is described in the motivational example section of Langfelder P, Horvath S (2012) Fast R Functions for Robust Correlations and Hierarchical Clustering. Journal of Statistical Software 46(11) 1-17; PMID: 23050260 PMCID: PMC3465711

See Also

blockwiseModules for the underlying network analysis and module identification; sampledHierarchicalConsensusModules for a similar resampling analysis of consensus networks.

sampledHierarchicalConsensusModules

Hierarchical consensus module identification in sampled data

Description

This function repeatedly resamples the samples (rows) in supplied data and identifies hierarchical consensus modules on the resampled data.

Usage

```
sampledHierarchicalConsensusModules(
 multiExpr,
 multiWeights = NULL,
 networkOptions,
  consensusTree,
 nRuns,
  startRunIndex = 1,
  endRunIndex = startRunIndex + nRuns -1,
  replace = FALSE,
  fraction = if (replace) 1.0 else 0.63,
  randomSeed = 12345,
  checkSoftPower = TRUE,
  nPowerCheckSamples = 2000,
  individualTOMFilePattern = "individualTOM-Run.%r-Set%s-Block.%b.RData",
  keepConsensusTOMs = FALSE,
  consensusTOMFilePattern = "consensusTOM-Run.%r-%a-Block.%b.RData",
  skipUnsampledCalculation = FALSE,
  verbose = 2, indent = 0,
```

```
saveRunningResults = TRUE,
runningResultsFile = "results.tmp.RData")
```

Arguments

multiExpr Expression data in the multi-set format (see checkSets). A vector of lists, one

per set. Each set must contain a component data that contains the expression data, with rows corresponding to samples and columns to genes or probes.

multiWeights optional observation weights in the same format (and dimensions) as multiExpr.

These weights are used for correlation calculations with data in multiExpr.

networkOptions A single list of class NetworkOptions giving options for network calculation

for all of the networks, or a multiData structure containing one such list for

each input data set.

consensusTree A list specifying the consensus calculation. See details.

nRuns Number of network construction and module identification runs.

startRunIndex Number to be assigned to the start run. The run number or index is used to make

saved files unique; it has no effect on the actual results of the run.

endRunIndex Number (index) of the last run. If given, nRuns is ignored.

replace Logical: should samples (observations or rows in entries in multiExpr) be sam-

pled with replacement?

fraction Fraction of samples to sample for each run.

randomSeed Integer specifying the random seed. If non-NULL, the random number genera-

tor state is saved before the seed is set and restored at the end of the function. If NULL, the random number generator state is not changed nor saved at the start,

and not restored at the end.

checkSoftPower Logical: should the soft-tresholding power be adjusted to approximately match

the connectivity distribution of the sampled data set and the full data set?

nPowerCheckSamples

Number of genes to be sampled from the full data set to calculate connectivity

and match soft-tresholding powers.

individualTOMFilePattern

Pattern for file names for files holding individual TOMs. The tags "%r, %a, %b" are replaced by run number, analysis name and block number, respectively. The TOM files are usually temporary but can be retained, see keepConsensusTOM

below.

keepConsensusTOMs

Logical: should the (final) consensus TOMs of each sampled calculation be retained after the run ends? Note that for large data sets (tens of thousands of

nodes) the TOM files are rather large.

consensusTOMFilePattern

Pattern for file names for files holding consensus TOMs. The tags "%r , %a , %b" are replaced by run number, analysis name and block number, respectively. The TOM files are usually temporary but can be retained, see keepConsensusTOM

above.

skipUnsampledCalculation

Logical: should a calculation on original (not resampled) data be skipped?

... Other arguments to hierarchicalConsensusModules.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

saveRunningResults

Logical: should the cumulative results be saved after each run on resampled

data?

runningResultsFile

File name of file in which to save running results into. In case of a parallel execution (say on several nodes of a cluster), one should choose a unique name

for each process to avoid overwriting the same file.

Details

For each run, samples (but not genes) are randomly sampled to obtain a perturbed data set; a full network analysis and module identification is carried out, and the results are returned in a list with one component per run.

For each run, the soft-thresholding power can optionally be adjusted such that the mean adjacency in the re-sampled data set equals the mean adjacency in the original data.

Value

A list with one component per run. Each component is a list with the following components:

mods The output of the function hierarchicalConsensusModules on the resampled

data.

samples Indices of the samples selected for the resampled data step for this run.

powers Actual soft-thresholding powers used in this run.

Author(s)

Peter Langfelder

See Also

hierarchicalConsensusModules for consensus networ analysis and module identification; sampledBlockwiseModules for a similar resampling analysis for a single data set.

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scaleFreeFitIndex	Calculation of fitting statistics for evaluating scale free topology fit.

Description

The function scaleFreeFitIndex calculates several indices (fitting statistics) for evaluating scale free topology fit. The input is a vector (of connectivities) k. Next k is discretized into nBreaks number of equal-width bins. Let's denote the resulting vector dk. The relative frequency for each bin is denoted p.dk.

Usage

```
scaleFreeFitIndex(k, nBreaks = 10, removeFirst = FALSE)
```

Arguments

k numeric vector whose components contain non-negative values nBreaks positive integer. This determines the number of equal width bins.

removeFirst logical. If TRUE then the first bin will be removed.

Value

Data frame with columns

Rsquared.SFT the model fitting index (R.squared) from the following model lm(log.p.dk ~

log.dk)

slope.SFT the slope estimate from model $lm(log(p(k)) \sim log(k))$

 $truncated {\tt Exponential Adj Rsquared}$

the adjusted R.squared measure from the truncated exponential model given by

 $lm2 = lm(log.p.dk \sim log.dk + dk).$

Author(s)

Steve Horvath

Visual check of scale-free topology

Description

A simple visula check of scale-free network ropology.

scaleFreePlot 361

Usage

```
scaleFreePlot(
  connectivity,
  nBreaks = 10,
  truncated = FALSE,
  removeFirst = FALSE,
  main = "", ...)
```

Arguments

connectivity vector containing network connectivities.

nBreaks number of breaks in the connectivity dendrogram.

truncated logical: should a truncated exponential fit be calculated and plotted in addition

to the linear one?

removeFirst logical: should the first bin be removed from the fit?

main title for the plot.

... other graphical parameter to the plot function.

Details

The function plots a log-log plot of a histogram of the given connectivities, and fits a linear model plus optionally a truncated exponential model. The \mathbb{R}^2 of the fit can be considered an index of the scale freedom of the network topology.

Value

None.

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

softConnectivity for connectivity calculation in weighted networks.

SCsLists

Stem Cell-Related Genes with Corresponding Gene Markers

Description

This matrix gives a predefined set of genes related to several stem cell (SC) types, as reported in two previously-published studies. It is used with userListEnrichment to search user-defined gene lists for enrichment.

Usage

```
data(SCsLists)
```

Format

A 14003 x 2 matrix of characters containing Gene / Category pairs. The first column (Gene) lists genes corresponding to a given category (second column). Each Category entry is of the form <Stem cell-related category>__<reference>, where the references can be found at userListEnrichment. Note that the matrix is sorted first by Category and then by Gene, such that all genes related to the same category are listed sequentially.

Source

For references used in this variable, please see userListEnrichment

Examples

```
data(SCsLists)
head(SCsLists)
```

selectFewestConsensusMissing

Select columns with the lowest consensus number of missing data

Description

Given a multiData structure, this function calculates the consensus number of present (non-missing) data for each variable (column) across the data sets, forms the consensus and for each group selects variables whose consensus proportion of present data is at least selectFewestMissing (see usage below).

Usage

```
selectFewestConsensusMissing(
   mdx,
   colID,
   group,
   minProportionPresent = 1,
   consensusQuantile = 0,
   verbose = 0,
   ...)
```

Arguments

mdx A multiData structure. All sets must have the same columns.

colID Character vector of column identifiers. This must include all the column names

from mdx, but can include other values as well. Its entries must be unique (no

duplicates) and no missing values are permitted.

group Character vector whose components contain the group label (e.g. a character

string) for each entry of colID. This vector must be of the same length as the vector colID. In gene expression applications, this vector could contain the gene

symbol (or a co-expression module label).

minProportionPresent

A numeric value between 0 and 1 (logical values will be coerced to numeric). Denotes the minimum consensus fraction of present data in each column that

will result in the column being retained.

consensusQuantile

A number between 0 and 1 giving the quantile probability for consensus calcu-

lation. 0 means the minimum value (true consensus) will be used.

verbose Level of verbosity; 0 means silent, larger values will cause progress messages

to be printed.

... Other arguments that should be considered undocumented and subject to change.

Details

A 'consensus' of a vector (say 'x') is simply defined as the quantile with probability consensusQuantile of the vector x. This function calculates, for each variable in mdx, its proportion of present (i.e., non-NA and non-NaN) values in each of the data sets in mdx, and forms the consensus. Only variables whose consensus proportion of present data is at least selectFewestMissing are retained.

Value

A logical vector with one element per variable in mdx, giving TRUE for the retained variables.

Author(s)

Jeremy Miller and Peter Langfelder

setCorrelationPreservation

See Also

multiData

```
setCorrelationPreservation
```

Summary correlation preservation measure

Description

Given consensus eigengenes, the function calculates the average correlation preservation pair-wise for all pairs of sets.

Usage

```
setCorrelationPreservation(
   multiME,
   setLabels,
   excludeGrey = TRUE, greyLabel = "grey",
   method = "absolute")
```

Arguments

multiME	consensus module eigengenes in a multi-set format. A vector of lists with one
	list corresponding to each set. Each list must contain a component data that is

a data frame whose columns are consensus module eigengenes.

setLabels names to be used for the sets represented in multiME.

excludeGrey logical: exclude the 'grey' eigengene from preservation measure?

greyLabel module label corresponding to the 'grey' module. Usually this will be the char-

acter string "grey" if the labels are colors, and the number 0 if the labels are

numeric.

method character string giving the correlation preservation measure to use. Recognized

values are (unique abbreviations of) "absolute", "hyperbolic".

Details

For each pair of sets, the function calculates the average preservation of correlation among the eigengenes. Two preservation measures are available, the abosolute preservation (high if the two correlations are similar and low if they are different), and the hyperbolically scaled preservation, which de-emphasizes preservation of low correlation values.

Value

A data frame with each row and column corresponding to a set given in multiME, containing the pairwise average correlation preservation values. Names and rownames are set to entries of setLabels.

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Author(s)

Peter Langfelder

References

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54

See Also

```
multiSetMEs for module eigengene calculation;
plotEigengeneNetworks for eigengene network visualization.
```

shortenStrings

Shorten given character strings by truncating at a suitable separator.

Description

This function shortens given character strings so they are not longer than a given maximum length.

Usage

mum length?

Arguments

strings	Character strings to be shortened.			
maxLength	Maximum length (number of characters) in the strings to be retained. See details for when the returned strings can exceed this length.			
minLength	Minimum length of the returned strings. See details.			
split	Character string giving the split at which the strings can be truncated. This can be a literal string or a regular expression (if the latter, fixed below must be set to FALSE).			
fixed	Logical: should split be interpreted as a literal specification (TRUE) or as a regular expression (FALSE)?			
ellipsis	Character string that will be appended to every shorten string, to indicate that the string has been shortened.			
countEllipsisInLength				
	Logical: should the length of the ellipsis count toward the minimum and maxi-			

Details

Strings whose length (number of characters) is at most maxLength are returned unchanged. For those that are longer, the function uses <code>gregexpr</code> to search for the occurrences of <code>split</code> in each given character string. If such occurrences are found at positions between <code>minLength</code> and <code>maxLength</code>, the string will be truncated at the last such <code>split</code>; otherwise, the string will be truncated at <code>maxLength</code>. The <code>ellipsis</code> is appended to each truncated string.

Value

A character vector of strings, shortened as necessary. If the input strings had non-NULL dimensions and dimnames, these are copied to the output.

Author(s)

Peter Langfelder

See Also

gregexpr, the workhorse pattern matching function formatLabels for splitting strings into multiple lines

sigmoidAdjacencyFunction

Sigmoid-type adacency function.

Description

Sigmoid-type function that converts a similarity to a weighted network adjacency.

Usage

```
sigmoidAdjacencyFunction(ss, mu = 0.8, alpha = 20)
```

Arguments

ss similarity, a number between 0 and 1. Can be given as a scalar, vector or a

matrix.

mu shift parameter. alpha slope parameter.

Details

The sigmoid adjacency function is defined as $1/(1 + \exp[-\alpha(ss - \mu)])$.

Value

Adjacencies returned in the same form as the input ss

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Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

signedKME

Signed eigengene-based connectivity

Description

Calculation of (signed) eigengene-based connectivity, also known as module membership.

Usage

```
signedKME(
  datExpr,
  datME,
  exprWeights = NULL,
  MEWeights = NULL,
  outputColumnName = "kME",
  corFnc = "cor",
  corOptions = "use = 'p'")
```

Arguments

datExpr a data frame containing the gene expression data. Rows correspond to samples

and columns to genes. Missing values are allowed and will be ignored.

datME a data frame containing module eigengenes. Rows correspond to samples and

columns to module eigengenes.

exprWeights optional weight matrix of observation weights for datExpr, of the same di-

mensions as datExpr. If given, the weights must be non-negative and will be passed on to the correlation function given in argument corFnc as argument

weights.x.

MEWeights optional weight matrix of observation weights for datME, of the same dimen-

sions as datME. If given, the weights must be non-negative and will be passed on to the correlation function given in argument corFnc as argument weights.y.

outputColumnName

a character string specifying the prefix of column names of the output.

corFnc character string specifying the function to be used to calculate co-expression

similarity. Defaults to Pearson correlation. Any function returning values be-

tween -1 and 1 can be used.

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corOptions

character string specifying additional arguments to be passed to the function given by corFnc. Use "use = 'p', method = 'spearman'" to obtain Spearman correlation.

Details

Signed eigengene-based connectivity of a gene in a module is defined as the correlation of the gene with the corresponding module eigengene. The samples in datExpr and datME must be the same.

Value

A data frame in which rows correspond to input genes and columns to module eigengenes, giving the signed eigengene-based connectivity of each gene with respect to each eigengene.

Author(s)

Steve Horvath

References

Dong J, Horvath S (2007) Understanding Network Concepts in Modules, BMC Systems Biology 2007, 1:24

Horvath S, Dong J (2008) Geometric Interpretation of Gene Coexpression Network Analysis. PLoS Comput Biol 4(8): e1000117

signifNumeric

Round numeric columns to given significant digits.

Description

This function applies link{signif} (or possibly other rounding function) to numeric, non-integer columns of a given data frame.

Usage

```
signifNumeric(x, digits, fnc = "signif")
```

Arguments

x Input data frame, matrix or matrix-like object that can be coerced to a data frame.

digits Significant digits to retain.

fnc The rounding function. Typically either signif or round.

Details

The function fnc is applied to each numeric column that contains at least one non-integer (i.e., at least one element that does not equal its own round).

Value

The transformed data frame.

Author(s)

Peter Langfelder

See Also

The rounding functions signif and round.

Examples

```
df = data.frame(text = letters[1:3], ints = c(1:3)+234, nonints = c(0:2) + 0.02345); df; signifNumeric(df, 2); signifNumeric(df, 2, fnc = "round");
```

signumAdjacencyFunction

Hard-thresholding adjacency function

Description

This function transforms correlations or other measures of similarity into an unweighted network adjacency.

Usage

```
signumAdjacencyFunction(corMat, threshold)
```

Arguments

corMat a matrix of correlations or other measures of similarity.

threshold threshold for connecting nodes: all nodes whose corMat is above the threshold

will be connected in the resulting network.

Value

An unweighted adjacency matrix of the same dimensions as the input corMat.

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

adjacency for soft-thresholding and creating weighted networks.

simpleConsensusCalculation

Simple calculation of a single consenus

Description

This function calculates a single consensus from given individual data.

Usage

```
simpleConsensusCalculation(
  individualData,
  consensusOptions,
  verbose = 1,
  indent = 0)
```

Arguments

individualData Individual data from which the consensus is to be calculated. It can be either a list or a multiData structure in which each element is a numeric vector or array.

consensusOptions

A list of class ConsensusOptions that contains options for the consensus calculation. A suitable list can be obtained by calling function newConsensusOptions.

verbose Integer level of verbosity of diagnostic messages. Zero means silent, higher

values make the output progressively more and more verbose.

indent Indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

Consensus is defined as the element-wise (also known as "parallel") quantile of of the individual data at probability given by the consensusQuantile element of consensusOptions.

Value

A numeric vector or array of the same dimensions as each element of individualData

Author(s)

Peter Langfelder

References

Consensus network analysis was originally described in Langfelder P, Horvath S. Eigengene networks for studying the relationships between co-expression modules. BMC Systems Biology 2007, 1:54 https://bmcsystbiol.biomedcentral.com/articles/10.1186/1752-0509-1-54

See Also

consensusCalculation for consensus calculation that can work with BlockwiseData and can calibrate data before calculating consensus.

 ${\it simple Hierarchical Consensus Calculation}$

Simple hierarchical consensus calculation

Description

Hierarchical consensus calculation without calibration.

Usage

simpleHierarchicalConsensusCalculation(individualData, consensusTree, level = 1)

Arguments

individualData Individual data from which the consensus is to be calculated. It can be either

a list or a multiData structure. Each element in individulData should be a

numeric object (vector, matrix or array).

consensusTree A list specifying the consensus calculation. See details.

level Integer which the user should leave at 1. This serves to keep default set names

unique.

Details

This function calculates consensus in a hierarchical manner, using a separate (and possibly different) set of consensus options at each step. The "recipe" for the consensus calculation is supplied in the argument consensusTree.

The argument consensusTree should have the following components: (1) inputs must be either a character vector whose components match names(inputData), or consensus trees in the own right. (2) consensusOptions must be a list of class "ConsensusOptions" that specifies options for calculating the consensus. A suitable set of options can be obtained by calling newConsensusOptions. (3) Optionally, the component analysisName can be a single character string giving the name for

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the analysis. When intermediate results are returned, they are returned in a list whose names will be set from analysisName components, if they exist.

Unlike the similar function hierarchicalConsensusCalculation, this function ignores the calibration settings in the consensusOptions component of consensusTree; no calibration of input data is performed.

The actual consensus calculation at each level of the consensus tree is carried out in function simpleConsensusCalculation. The consensus options for each individual consensus calculation are independent from one another, i.e., the consensus options for different steps can be different.

Value

A list with a single component consensus, containing the consensus data of the same dimensions as the individual entries in the input individualData. This perhaps somewhat cumbersome convention is used to make the output compatible with that of hierarchicalConsensusCalculation.

Author(s)

Peter Langfelder

See Also

simpleConsensusCalculation for a "single-level" consensus calculation; hierarchicalConsensusCalculation for hierarchical consensus calculation with calibration

simulateDatExpr

Simulation of expression data

Description

Simulation of expression data with a customizable modular structure and several different types of noise.

Usage

```
simulateDatExpr(
  eigengenes,
  nGenes,
  modProportions,
  minCor = 0.3,
  maxCor = 1,
  corPower = 1,
  signed = FALSE,
  propNegativeCor = 0.3,
  geneMeans = NULL,
  backgroundNoise = 0.1,
  leaveOut = NULL,
  nSubmoduleLayers = 0,
```

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```
nScatteredModuleLayers = 0,
averageNGenesInSubmodule = 10,
averageExprInSubmodule = 0.2,
submoduleSpacing = 2,
verbose = 1, indent = 0)
```

Arguments

eigengenes a data frame containing the seed eigengenes for the simulated modules. Rows

correspond to samples and columns to modules.

nGenes total number of genes to be simulated.

modProportions a numeric vector with length equal the number of eigengenes in eigengenes

plus one, containing fractions of the total number of genes to be put into each of the modules and into the "grey module", which means genes not related to any

of the modules. See details.

minCor minimum correlation of module genes with the corresponding eigengene. See

details.

maxCor maximum correlation of module genes with the corresponding eigengene. See

details.

corPower controls the dropoff of gene-eigengene correlation. See details.

signed logical: should the genes be simulated as belonging to a signed network? If

TRUE, all genes will be simulated to have positive correlation with the eigengene. If FALSE, a proportion given by propNegativeCor will be simulated with

negative correlations of the same absolute values.

propNegativeCor

proportion of genes to be simulated with negative gene-eigengene correlations.

Only effective if signed is FALSE.

geneMeans optional vector of length nGenes giving desired mean expression for each gene.

If not given, the returned expression profiles will have mean zero.

backgroundNoise

amount of background noise to be added to the simulated expression data.

leaveOut optional specification of modules that should be left out of the simulation, that

is their genes will be simulated as unrelated ("grey"). This can be useful when simulating several sets, in some which a module is present while in others it is

absent.

nSubmoduleLayers

number of layers of ordered submodules to be added. See details.

nScatteredModuleLayers

number of layers of scattered submodules to be added. See details.

averageNGenesInSubmodule

average number of genes in a submodule. See details.

averageExprInSubmodule

average strength of submodule expression vectors.

submoduleSpacing

a number giving submodule spacing: this multiple of the submodule size will lie between the submodule and the next one.

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verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

Given eigengenes can be unrelated or they can exhibit non-trivial correlations. Each module is simulated separately from others. The expression profiles are chosen such that their correlations with the eigengene run from just below maxCor to minCor (hence minCor must be between 0 and 1, not including the bounds). The parameter corPower can be chosen to control the behaviour of the simulated correlation with the gene index; values higher than 1 will result in the correlation approaching minCor faster and lower than 1 slower.

Numbers of genes in each module are specified (as fractions of the total number of genes nGenes) by modProportions. The last entry in modProportions corresponds to the genes that will be simulated as unrelated to anything else ("grey" genes). The proportion must add up to 1 or less. If the sum is less than one, the remaining genes will be partitioned into groups and simulated to be "close" to the proper modules, that is with small but non-zero correlations (between minCor and 0) with the module eigengene.

If signed is set FALSE, the correlation for some of the module genes is chosen negative (but the absolute values remain the same as they would be for positively correlated genes). To ensure consistency for simulations of multiple sets, the indices of the negatively correlated genes are fixed and distributed evenly.

In addition to the primary module structure, a secondary structure can be optionally simulated. Modules in the secondary structure have sizes chosen from an exponential distribution with mean equal averageNGenesInSubmodule. Expression vectors simulated in the secondary structure are simulated with expected standard deviation chosen from an exponential distribution with mean equal averageExprInSubmodule; the higher this coefficient, the more pronounced will the submodules be in the main modules. The secondary structure can be simulated in several layers; their number is given by SubmoduleLayers. Genes in these submodules are ordered in the same order as in the main modules.

In addition to the ordered submodule structure, a scattered submodule structure can be simulated as well. This structure can be viewed as noise that tends to correlate random groups of genes. The size and effect parameters are the same as for the ordered submodules, and the number of layers added is controlled by nScatteredModuleLayers.

Value

A list with the following components:

datExpr simulated expression data in a data frame whose columns correspond genes and

rows to samples.

setLabels simulated module assignment. Module labels are numeric, starting from 1.

Genes simulated to be outside of proper modules have label 0. Modules that

are left out (specified in leaveOut) are indicated as 0 here.

allLabels simulated module assignment. Genes that belong to leftout modules (specified

in leaveOut) are indicated by their would-be assignment here.

labelOrder

a vector specifying the order in which labels correspond to the given eigengenes, that is labelOrder[1] is the label assigned to module whose seed is eigengenes[, 1] etc.

Author(s)

Peter Langfelder

References

A short description of the simulation method can also be found in the Supplementary Material to the article

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54.

The material is posted at http://horvath.genetics.ucla.edu/html/CoexpressionNetwork/EigengeneNetwork/SupplementSimula

See Also

```
simulateEigengeneNetwork for a simulation of eigengenes with a given causal structure; simulateModule for simulations of individual modules; simulateDatExpr5Modules for a simplified interface to expression simulations; simulateMultiExpr for a simulation of several related data sets.
```

simulateDatExpr5Modules

Simplified simulation of expression data

Description

This function provides a simplified interface to the expression data simulation, at the cost of considerably less flexibility.

Usage

```
simulateDatExpr5Modules(
   nGenes = 2000,
   colorLabels = c("turquoise", "blue", "brown", "yellow", "green"),
   simulateProportions = c(0.1, 0.08, 0.06, 0.04, 0.02),
   MEturquoise, MEblue, MEbrown, MEyellow, MEgreen,
   SDnoise = 1, backgroundCor = 0.3)
```

Arguments

nGenes total number of genes to be simulated.

colorLabels labels for simulated modules.

simulateProportions

a vector of length 5 giving proportions of the total number of genes to be placed in each individual module. The entries must be positive and sum to at most 1. If the sum is less than 1, the leftover genes will be simulated outside of modules.

MEturquoise seed module eigengene for the first module.

MEblue seed module eigengene for the second module.

MEbrown seed module eigengene for the third module.

MEyellow seed module eigengene for the fourth module.

MEgreen seed module eigengene for the fifth module.

SDnoise level of noise to be added to the simulated expressions.

backgroundCor background correlation. If non-zero, a component will be added to all genes such

that the average correlation of otherwise unrelated genes will be backgroundCor.

Details

Roughly one-third of the genes are simulated with a negative correlation to their seed eigengene. See the functions simulateModule and simulateDatExpr for more details.

Value

A list with the following components:

datExpr the simulated expression data in a data frame, with rows corresponding to sam-

ples and columns to genes.

truemodule a vector with one entry per gene containing the simulated module membership.

datME a data frame containing a copy of the input module eigengenes.

Author(s)

Steve Horvath and Peter Langfelder

See Also

simulateModule for simulation of individual modules;

simulateDatExpr for a more comprehensive data simulation interface.

simulate Eigengene Network

Simulate eigengene network from a causal model

Description

Simulates a set of eigengenes (vectors) from a given set of causal anchors and a causal matrix.

Usage

```
simulateEigengeneNetwork(
  causeMat,
  anchorIndex, anchorVectors,
  noise = 1,
  verbose = 0, indent = 0)
```

Arguments

causeMat causal matrix. The entry [i,j] is the influence (path coefficient) of vector j on

vector i.

anchorIndex specifies the indices of the anchor vectors.

anchorVectors a matrix giving the actual anchor vectors as columns. Their number must equal

the length of anchorIndex.

noise standard deviation of the noise added to each simulated vector.

verbose level of verbosity. 0 means silent.

indent indentation for diagnostic messages. Zero means no indentation; each unit adds

two spaces.

Details

The algorithm starts with the anchor vectors and iteratively generates the rest from the path coefficients given in the matrix causeMat.

Value

A list with the following components:

eigengenes generated eigengenes.

causeMat a copy of the input causal matrix

levels useful for debugging. A vector with one entry for each eigengene giving the

number of generations of parents of the eigengene. Anchors have level 0, their

direct causal children have level 1 etc.

anchorIndex a copy of the input anchorIndex.

Author(s)

Peter Langfelder

378 simulateModule

eModule Simulate a gene co-expression module
--

Description

Simulation of a single gene co-expression module.

Usage

```
simulateModule(
    ME,
    nGenes,
    nNearGenes = 0,
    minCor = 0.3, maxCor = 1, corPower = 1,
    signed = FALSE, propNegativeCor = 0.3,
    geneMeans = NULL,
    verbose = 0, indent = 0)
```

Arguments

	1 11 .
ME	seed module eigengene
l'IL	seed module eigengene.

nGenes number of genes in the module to be simulated. Must be non-zero.

nNearGenes number of genes to be simulated with low correlation with the seed eigengene.

minCor minimum correlation of module genes with the eigengene. See details.

maxCor maximum correlation of module genes with the eigengene. See details.

corPower controls the dropoff of gene-eigengene correlation. See details.

signed logical: should the genes be simulated as belonging to a signed network? If

TRUE, all genes will be simulated to have positive correlation with the eigengene. If FALSE, a proportion given by propNegativeCor will be simulated with

negative correlations of the same absolute values.

propNegativeCor

proportion of genes to be simulated with negative gene-eigengene correlations.

Only effective if signed is FALSE.

geneMeans optional vector of length nGenes giving desired mean expression for each gene.

If not given, the returned expression profiles will have mean zero.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

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Details

Module genes are simulated around the eigengene by choosing them such that their (expected) correlations with the seed eigengene decrease progressively from (just below) maxCor to minCor. The genes are otherwise independent from one another. The variable corPower determines how fast the correlation drops towards minCor. Higher powers lead to a faster frop-off; corPower must be above zero but need not be integer.

If signed is FALSE, the genes are simulated so as to be part of an unsigned network module, that is some genes will be simulated with a negative correlation with the seed eigengene (but of the same absolute value that a positively correlated gene would be simulated with). The proportion of genes with negative correlation is controlled by propNegativeCor.

Optionally, the function can also simulate genes that are "near" the module, meaning they are simulated with a low but non-zero correlation with the seed eigengene. The correlations run between minCor and zero.

Value

A matrix containing the expression data with rows corresponding to samples and columns to genes.

Author(s)

Peter Langfelder

References

A short description of the simulation method can also be found in the Supplementary Material to the article

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54.

The material is posted at http://horvath.genetics.ucla.edu/html/CoexpressionNetwork/EigengeneNetwork/SupplementSimula

See Also

```
{\tt simulateEigengeneNetwork}\ for\ a\ simulation\ of\ eigengenes\ with\ a\ given\ causal\ structure;
```

simulateDatExpr for simulations of whole datasets consisting of multiple modules;

simulateDatExpr5Modules for a simplified interface to expression simulations;

simulateMultiExpr for a simulation of several related data sets.

simulateMultiExpr

Simulate multi-set expression data

Description

Simulation of expression data in several sets with relate module structure.

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Usage

```
simulateMultiExpr(eigengenes,
                  nGenes,
                  modProportions,
                  minCor = 0.5, maxCor = 1,
                  corPower = 1,
                  backgroundNoise = 0.1,
                  leaveOut = NULL,
                  signed = FALSE,
                  propNegativeCor = 0.3,
                  geneMeans = NULL,
                  nSubmoduleLayers = 0,
                  nScatteredModuleLayers = 0,
                  averageNGenesInSubmodule = 10,
                  averageExprInSubmodule = 0.2,
                  submoduleSpacing = 2,
                  verbose = 1, indent = 0)
```

Arguments

eigengenes the seed eigengenes for the simulated modules in a multi-set format. A list with

one component per set. Each component is again a list that must contain a component data. This is a data frame of seed eigengenes for the corresponding data set. Columns correspond to modules, rows to samples. Number of samples in the simulated data is determined from the number of samples of the eigengenes.

nGenes integer specifyin the number of simulated genes.

a numeric vector with length equal the number of eigengenes in eigengenes modProportions

> plus one, containing fractions of the total number of genes to be put into each of the modules and into the "grey module", which means genes not related to any

of the modules. See details.

minCor minimum correlation of module genes with the corresponding eigengene. See

details.

maxCor maximum correlation of module genes with the corresponding eigengene. See

corPower controls the dropoff of gene-eigengene correlation. See details.

backgroundNoise

amount of background noise to be added to the simulated expression data.

leaveOut optional specification of modules that should be left out of the simulation, that

is their genes will be simulated as unrelated ("grey"). A logical matrix in which columns correspond to sets and rows to modules. Wherever TRUE, the corresponding module in the corresponding data set will not be simulated, that is its

genes will be simulated independently of the eigengene.

signed logical: should the genes be simulated as belonging to a signed network? If

> TRUE, all genes will be simulated to have positive correlation with the eigengene. If FALSE, a proportion given by propNegativeCor will be simulated with

negative correlations of the same absolute values.

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propNegativeCor

proportion of genes to be simulated with negative gene-eigengene correlations.

Only effective if signed is FALSE.

geneMeans optional vector of length nGenes giving desired mean expression for each gene.

If not given, the returned expression profiles will have mean zero.

nSubmoduleLayers

number of layers of ordered submodules to be added. See details.

nScatteredModuleLayers

number of layers of scattered submodules to be added. See details.

averageNGenesInSubmodule

average number of genes in a submodule. See details.

averageExprInSubmodule

average strength of submodule expression vectors.

submoduleSpacing

a number giving submodule spacing: this multiple of the submodule size will

lie between the submodule and the next one.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

For details of simulation of individual data sets and the meaning of individual set simulation arguments, see simulateDatExpr. This function simulates several data sets at a time and puts the result in a multi-set format. The number of genes is the same for all data sets. Module memberships are also the same, but modules can optionally be "dissolved", that is their genes will be simulated as unassigned. Such "dissolved", or left out, modules can be specified in the matrix leaveOut.

Value

A list with the following components:

multiExpr simulated expression data in multi-set format analogous to that of the input

eigengenes. A list with one component per set. Each component is again a list that must contains a component data. This is a data frame of expression data for the corresponding data set. Columns correspond to genes, rows to sam-

ples.

setLabels a matrix of dimensions (number of genes) times (number of sets) that contains

module labels for each genes in each simulated data set.

allLabels a matrix of dimensions (number of genes) times (number of sets) that contains

the module labels that would be simulated if no module were left out using leaveOut. This means that all columns of the matrix are equal; the columns are repeated for convenience so allLabels has the same dimensions as setLabels.

labelOrder a matrix of dimensions (number of modules) times (number of sets) that contains

the order in which module labels were assigned to genes in each set. The first label is assigned to genes 1...(module size of module labeled by first label), the

second label to the following batch of genes etc.

382 simulateSmallLayer

Author(s)

Peter Langfelder

References

A short description of the simulation method can also be found in the Supplementary Material to the article

Langfelder P, Horvath S (2007) Eigengene networks for studying the relationships between coexpression modules. BMC Systems Biology 2007, 1:54.

The material is posted at http://horvath.genetics.ucla.edu/html/CoexpressionNetwork/EigengeneNetwork/SupplementSimula

See Also

```
simulateEigengeneNetwork for a simulation of eigengenes with a given causal structure;
simulateDatExpr for simulation of individual data sets;
simulateDatExpr5Modules for a simple simulation of a data set consisting of 5 modules;
simulateModule for simulations of individual modules;
```

simulateSmallLayer

Simulate small modules

Description

This function simulates a set of small modules. The primary purpose is to add a submodule structure to the main module structure simulated by simulateDatExpr.

Usage

```
simulateSmallLayer(
  order,
  nSamples,
  minCor = 0.3, maxCor = 0.5, corPower = 1,
  averageModuleSize,
  averageExpr,
  moduleSpacing,
  verbose = 4, indent = 0)
```

Arguments

order a vector giving the simulation order for vectors. See details.

nSamples integer giving the number of samples to be simulated.

minCor a multiple of maxCor (see below) giving the minimum correlation of module

genes with the corresponding eigengene. See details.

maxCor maximum correlation of module genes with the corresponding eigengene. See

details.

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corPower controls the dropoff of gene-eigengene correlation. See details.

averageModuleSize

average number of genes in a module. See details.

averageExpr average strength of module expression vectors.

moduleSpacing a number giving module spacing: this multiple of the module size will lie be-

tween the module and the next one.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

Module eigenvectors are chosen randomly and independently. Module sizes are chosen randomly from an exponential distribution with mean equal averageModuleSize. Two thirds of genes in each module are simulated as proper module genes and one third as near-module genes (see simulateModule for details). Between each successive pairs of modules a number of genes given by moduleSpacing will be left unsimulated (zero expression). Module expression, that is the expected standard deviation of the module expression vectors, is chosen randomly from an exponential distribution with mean equal averageExpr. The expression profiles are chosen such that their correlations with the eigengene run from just below maxCor to minCor * maxCor (hence minCor must be between 0 and 1, not including the bounds). The parameter corPower can be chosen to control the behaviour of the simulated correlation with the gene index; values higher than 1 will result in the correlation approaching minCor * maxCor faster and lower than 1 slower.

The simulated genes will be returned in the order given in order.

Value

A matrix of simulated gene expressions, with dimension (nSamples, length(order)).

Author(s)

Peter Langfelder

See Also

simulateModule for simulation of individual modules;

simulateDatExpr for the main gene expression simulation function.

sizeGrWindow

Opens a graphics window with specified dimensions

Description

If a graphic device window is already open, it is closed and re-opened with specified dimensions (in inches); otherwise a new window is opened.

Usage

```
sizeGrWindow(width, height)
```

Arguments

width desired width of the window, in inches. height desired heigh of the window, in inches.

Value

None.

Author(s)

Peter Langfelder

sizeRestrictedClusterMerge

Cluter merging with size restrictions

Description

This function merges clusters by correlation of the first principal components such that the resulting merged clusters do not exceed a given maximum size.

Usage

```
sizeRestrictedClusterMerge(
    datExpr,
    clusters,
    clusterSizes = NULL,
    centers = NULL,
    maxSize,
    networkType = "unsigned",
    verbose = 0,
    indent = 0)
```

Arguments

datExpr	Data on which the clustering is based (e.g., expression data). Variables are in columns and observations (samples) in rows.			
clusters	A vector with element per variable (column) in datExpr giving the cluster label for the corresponding variable.			
clusterSizes	Optional pre-calculated cluster sizes. If not given, will be determined from given clusters.			
centers	Optional pre-calculaed cluster centers (first principal components/singular vectors). If not given, will be calculated from given data and cluster assignments.			
maxSize	Maximum allowed size of merged clusters. If any of the given clusters are larger than maxSize, they will not be changed.			
networkType	One of "unsigned" and "signed". Determines whether clusters with negatively correlated representatives will be considered similar ("unsigned") or dissimilar ("signed").			
verbose	integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.			
indent	indentation for diagnostic messages. Zero means no indentation, each unit adds two spaces.			

Details

The function iteratively merges two closest clusters subject to the constraint that the merged cluster size cannot exceed maxSize. Merging stops when no two clusters can be merged without exceeding the maximum size.

Value

A list with two components

clusters A numeric vector with one component per input gene, giving the cluster number

in which the gene is assigned.

centers Cluster centers, that is their first principal components/singular vectors.

Author(s)

Peter Langfelder

See Also

The last step in projectiveKMeans uses this function.

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softConnectivity

Calculates connectivity of a weighted network.

Description

Given expression data or a similarity, the function constructs the adjacency matrix and for each node calculates its connectivity, that is the sum of the adjacency to the other nodes.

Usage

```
softConnectivity(
  datExpr,
  corFnc = "cor", corOptions = "use = 'p'",
  weights = NULL,
  type = "unsigned",
  power = if (type == "signed") 15 else 6,
  blockSize = 1500,
  minNSamples = NULL,
  verbose = 2, indent = 0)

softConnectivity.fromSimilarity(
  similarity,
  type = "unsigned",
  power = if (type == "signed") 15 else 6,
  blockSize = 1500,
  verbose = 2, indent = 0)
```

Arguments

datExpr	a data frame containing the expression data, with rows corresponding to samples and columns to genes.	
similarity	a similarity matrix: a square symmetric matrix with entries between -1 and 1.	
corFnc	character string giving the correlation function to be used for the adjacency calculation. Recommended choices are "cor" and "bicor", but other functions can be used as well.	
corOptions	character string giving further options to be passed to the correlation function.	
weights	optional observation weights for datExpr to be used in correlation calculation. A matrix of the same dimensions as datExpr, containing non-negative weights. Only used with Pearson correlation.	
type	network type. Allowed values are (unique abbreviations of) "unsigned", "signed" "signed hybrid".	
power	soft thresholding power.	

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blockSize block size in which adjacency is to be calculated. Too low (say below 100)

may make the calculation inefficient, while too high may cause R to run out of physical memory and slow down the computer. Should be chosen such that an array of doubles of size (number of genes) * (block size) fits into available

physical memory.

minNSamples minimum number of samples available for the calculation of adjacency for the

adjacency to be considered valid. If not given, defaults to the greater of ..minNSamples (currently 4) and number of samples divided by 3. If the number of samples falls below this threshold, the connectivity of the corresponding gene will be returned

as NA.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Value

A vector with one entry per gene giving the connectivity of each gene in the weighted network.

Author(s)

Steve Horvath

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

adjacency

spaste Space-less paste

Description

A convenient wrapper for the paste function with sep="".

Usage

```
spaste(...)
```

Arguments

... standard arguments to function paste except sep.

388 standardColors

Value

The result of the corresponding paste.

Note

Do not use the sep argument. Using will lead to an error.

Author(s)

Peter Langfelder

See Also

```
paste
```

Examples

```
a = 1;
paste("a=", a);
spaste("a=", a);
```

standardColors

Colors this library uses for labeling modules.

Description

Returns the vector of color names in the order they are assigned by other functions in this library.

Usage

```
standardColors(n = NULL)
```

Arguments

n

Number of colors requested. If NULL, all (approx. 450) colors will be returned. Any other invalid argument such as less than one or more than maximum (length(standardColors())) will trigger an error.

Value

A vector of character color names of the requested length.

Author(s)

```
Peter Langfelder, <Peter.Langfelder@gmail.com>
```

Examples

```
standardColors(10);
```

```
standard Screening Binary Trait\\
```

Standard screening for binatry traits

Description

The function standardScreeningBinaryTrait computes widely used statistics for relating the columns of the input data frame (argument datE) to a binary sample trait (argument y). The statistics include Student t-test p-value and the corresponding local false discovery rate (known as q-value, Storey et al 2004), the fold change, the area under the ROC curve (also known as C-index), mean values etc. If the input option KruskalTest is set to TRUE, it also computes the Kruskal Wallist test p-value and corresponding q-value. The Kruskal Wallis test is a non-parametric, rank-based group comparison test.

Usage

```
standardScreeningBinaryTrait(
    datExpr, y,
    corFnc = cor, corOptions = list(use = 'p'),
    kruskalTest = FALSE, qValues = FALSE,
    var.equal=FALSE, na.action="na.exclude",
    getAreaUnderROC = TRUE)
```

Arguments

datExpr	a data frame or	matrix whose col	lumns will be relate	ed to the binary trait
---------	-----------------	------------------	----------------------	------------------------

y a binary vector whose length (number of components) equals the number of

rows of datE

corFnc correlation function. Defaults to Pearson correlation.

corOptions a list specifying options to corFnc. An empty list must be specified as list()

(supplying NULL instead will trigger an error).

kruskalTest logical: should the Kruskal test be performed?

qValues logical: should the q-values be calculated?

var.equal logical input parameter for the Student t-test. It indicates whether to treat the

two variances (corresponding to the binary grouping) are being equal. If TRUE then the pooled variance is used to estimate the variance otherwise the Welch (or Satterthwaite) approximation to the degrees of freedom is used. Warning: here the default value is TRUE which is different from the default value of t.test.

Type help(t.test) for more details.

na.action character string for the Student t-test: indicates what should happen when the

data contain missing values NAs.

getAreaUnderROC

logical: should area under the ROC curve be calculated? The calculation slows

the function down somewhat.

Value

A data frame whose rows correspond to the columns of datE and whose columns report

ID column names of the input datExpr.

corPearson pearson correlation with a binary numeric version of the input variable. The

numeric variable equals 1 for level 1 and 2 for level 2. The levels are given by

levels(factor(y)).

t. Student's t-test statistic

pvalueStudent two-sided Student t-test p-value.

qvalueStudent (if input qValues==TRUE) q-value (local false discovery rate) based on the Stu-

dent T-test p-value (Storey et al 2004).

foldChange a (signed) ratio of mean values. If the mean in the first group (correspond-

ing to level 1) is larger than that of the second group, it equals meanFirst-Group/meanSecondGroup. But if the mean of the second group is larger than that of the first group it equals -meanSecondGroup/meanFirstGroup (notice the

minus sign).

meanFirstGroup means of columns in input datExpr across samples in the first group.

meanSecondGroup

means of columns in input datExpr across samples in the second group.

SE.FirstGroup standard errors of columns in input datExpr across samples in the first group.

Recall that $SE(x)=\operatorname{sqrt}(\operatorname{var}(x)/n)$ where n is the number of non-missing values of

х.

SE. SecondGroup standard errors of columns in input datExpr across samples in the second group.

areaUnderROC the area under the ROC, also known as the concordance index or C.index. This

is a measure of discriminatory power. The measure lies between 0 and 1 where 0.5 indicates no discriminatory power. 0 indicates that the "opposite" predictor has perfect discriminatory power. To compute it we use the function rcorr.cens with outx=TRUE (from Frank Harrel's package Hmisc). Only present if input

getAreUnderROC is TRUE.

nPresentSamples

number of samples with finite measurements for each gene.

If input kruskalTest is TRUE, the following columns further summarize results of Kruskal-Wallis test:

stat.Kruskal Kruskal-Wallis test statistic.

stat.Kruskal.signed

(Warning: experimental) Kruskal-Wallis test statistic including a sign that indicates whether the average rank is higher in second group (positive) or first group

(negative).

pvaluekruskal Kruskal-Wallis test p-values.

qkruskal q-values corresponding to the Kruskal-Wallis test p-value (if input qValues==TRUE).

Author(s)

Steve Horvath

References

Storey JD, Taylor JE, and Siegmund D. (2004) Strong control, conservative point estimation, and simultaneous conservative consistency of false discovery rates: A unified approach. Journal of the Royal Statistical Society, Series B, 66: 187-205.

Examples

```
require(survival) # For is.Surv in rcorr.cens
m=50
y=sample(c(1,2),m,replace=TRUE)
datExprSignal=simulateModule(scale(y),30)
datExprNoise=simulateModule(rnorm(m),150)
datExpr=data.frame(datExprSignal,datExprNoise)

Result1=standardScreeningBinaryTrait(datExpr,y)
Result1[1:5,]

# use unequal variances and calculate q-values
Result2=standardScreeningBinaryTrait(datExpr,y, var.equal=FALSE,qValue=TRUE)
Result2[1:5,]

# calculate Kruskal Wallis test and q-values
Result3=standardScreeningBinaryTrait(datExpr,y,kruskalTest=TRUE,qValue=TRUE)
Result3[1:5,]
```

standardScreeningCensoredTime

Standard Screening with regard to a Censored Time Variable

Description

The function standardScreeningCensoredTime computes association measures between the columns of the input data datE and a censored time variable (e.g. survival time). The censored time is specified using two input variables "time" and "event". The event variable is binary where 1 indicates that the event took place (e.g. the person died) and 0 indicates censored (i.e. lost to follow up). The function fits univariate Cox regression models (one for each column of datE) and outputs a Wald test p-value, a logrank p-value, corresponding local false discovery rates (known as q-values, Storey et al 2004), hazard ratios. Further it reports the concordance index (also know as area under the ROC curve) and optionally results from dichotomizing the columns of datE.

Usage

```
standardScreeningCensoredTime(
   time,
   event,
```

```
datExpr,
percentiles = seq(from = 0.1, to = 0.9, by = 0.2),
dichotomizationResults = FALSE,
qValues = TRUE,
fastCalculation = TRUE)
```

Arguments

time numeric variable showing time to event or time to last follow up.

event Input variable time specifies the time to event or time to last follow up. Input

variable event indicates whether the event happend (=1) or whether there was

censoring (=0).

datExpr a data frame or matrix whose columns will be related to the censored time.

percentiles numeric vector which is only used when dichotomizationResults=T. Each value

should lie between 0 and 1. For each value specified in the vector percentiles, a binary vector will be defined by dichotomizing the column value according to the corresponding quantile. Next a corresponding p-value will be calculated.

dichotomizationResults

logical. If this option is set to TRUE then the values of the columns of datE will be dichotomized and corresponding Cox regression p-values will be calculated.

qValues logical. If this option is set to TRUE (default) then q-values will be calculated

for the Cox regression p-values.

fastCalculation

logical. If set to TRUE, the function outputs correlation test p-values (and q-values) for correlating the columns of datE with the expected hazard (if no covariate is fit). Specifically, the expected hazard is defined as the deviance residual of an intercept only Cox regression model. The results are very similar to those resulting from a univariate Cox model where the censored time is regressed on the columns of dat. Specifically, this computational speed up is facilitated by the insight that the p-values resulting from a univariate Cox regression coxph(Surv(time,event)~datE[,i]) are very similar to those from cor-PvalueFisher(cor(devianceResidual,datE[,i]), nSamples).

Details

If input option fastCalculation=TRUE, then the function outputs correlation test p-values (and q-values) for correlating the columns of datE with the expected hazard (if no covariate is fit). Specifically, the expected hazard is defined as the deviance residual of an intercept only Cox regression model. The results are very similar to those resulting from a univariate Cox model where the censored time is regressed on the columns of dat. Specifically, this computational speed up is facilitated by the insight that the p-values resulting from a univariate Cox regression coxph(Surv(time,event)~datE[,i]) are very similar to those from corPvalueFisher(cor(devianceResidual,datE[,i]), nSamples)

Value

If fastCalculation is FALSE, the function outputs a data frame whose rows correspond to the columns of datE and whose columns report

ID column names of the input data datExpr.

pvalueWald Wald test p-value from fitting a univariate Cox regression model where the cen-

sored time is regressed on each column of datExpr.

qValueWald local false discovery rate (q-value) corresponding to the Wald test p-value.

pvalueLogrank Logrank p-value resulting from the Cox regression model. Also known as score

test p-value. For large sample sizes this sould be similar to the Wald test p-value.

qValueLogrank local false discovery rate (q-value) corresponding to the Logrank test p-value.

HazardRatio hazard ratio resulting from the Cox model. If the value is larger than 1, then high

values of the column are associated with shorter time, e.g. increased hazard of death. A hazard ratio equal to 1 means no relationship between the column and time. HR<1 means that high values are associated with longer time, i.e. lower

hazard.

CI.LowerLimitHR

Lower bound of the 95 percent confidence interval of the hazard ratio.

CI.UpperLimitHR

Upper bound of the 95 percent confidence interval of the hazard ratio.

C. index concordance index, also known as C-index or area under the ROC curve. Cal-

culated with the rcorr.cens option outx=TRUE (ties are ignored).

MinimumDichotPvalue

This is the smallest p-value from the dichotomization results. To see which dichotomized variable (and percentile) corresponds to the minimum, study the

following columns.

pValueDichot0.1

This columns report the p-value when the column is dichotomized according to the specified percentile (here 0.1). The percentiles are specified in the input

option percentiles.

pvalueDeviance The p-value resulting from using a correlation test to relate the expected hazard

(deviance residual) with each (undichotomized) column of datE. Specifically, the Fisher transformation is used to calculate the p-value for the Pearson correlation. The resulting p-value should be very similar to that of a univariate Cox

regression model.

qvalueDeviance Local false discovery rate (q-value) corresponding to pvalueDeviance.

corDeviance Pearson correlation between the expected hazard (deviance residual) with each

(undichotomized) column of datExpr.

Author(s)

Steve Horvath

standardScreeningNumericTrait

Standard screening for numeric traits

Description

Standard screening for numeric traits based on Pearson correlation.

Usage

Arguments

data frame containing expression data (or more generally variables to be screened),

with rows corresponding to samples and columns to genes (variables)

yNumeric a numeric vector giving the trait measurements for each sample

corFnc correlation function. Defaults to Pearson correlation but can also be bicor.

corOptions list specifying additional arguments to be passed to the correlation function

given by corFnc.

alternative alternative hypothesis for the correlation test

qValues logical: should q-values be calculated?

areaUnderROC logical: should are under the receiver-operating curve be calculated?

Details

The function calculates the correlations, associated p-values, area under the ROC, and q-values

Value

Data frame with the following components:

ID Gene (or variable) identifiers copied from colnames(datExpr)

cor correlations of all genes with the trait

Z Fisher Z statistics corresponding to the correlations

pvalueStudent Student p-values of the correlations

qvalueStudent (if input qValues==TRUE) q-values of the correlations calculated from the p-

values

AreaUnderROC (if input areaUnderROC==TRUE) area under the ROC

nPresentSamples

number of samples present for the calculation of each association.

stdErr 395

Author(s)

Steve Horvath

See Also

standard Screening Binary Trait, standard Screening Censored Time

stdErr

Standard error of the mean of a given vector.

Description

Returns the standard error of the mean of a given vector. Missing values are ignored.

Usage

```
stdErr(x)
```

Arguments

Χ

a numeric vector

Value

Standard error of the mean of x.

Author(s)

Steve Horvath

stratifiedBarplot

Bar plots of data across two splitting parameters

Description

This function takes an expression matrix which can be split using two separate splitting parameters (ie, control vs AD with multiple brain regions), and plots the results as a barplot. Group average, standard deviations, and relevant Kruskal-Wallis p-values are returned.

Usage

```
stratifiedBarplot(
  expAll,
  groups, split, subset,
  genes = NA,
  scale = "N", graph = TRUE,
  las1 = 2, cex1 = 1.5, ...)
```

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Arguments

expAll An expression matrix, with rows as samples and genes/probes as columns. If

genes=NA, then column names must be included.

groups A character vector corresponding to the samples in expAll, with each element

the group name of the relevant sample or NA for samples not in any group. For, example: NA, NA, NA, Con, Con, Con, Con, AD, AD, AD, AD, NA, NA. This

trait will be plotted as adjacent bars for each split.

split A character vector corresponding to the samples in expAll, with each element

the group splitting name of the relevant sample or NA for samples not in any group. For, example: NA, NA, NA, Hip, Hip, EC, EC, Hip, Hip, EC, EC, NA, NA. This trait will be plotted as the same color across each split of the barplot. For the function to work properly, the same split values should be inputted for

each group.

subset A list of one or more genes to compare the expression with. If the list contains

more than one gene, the first element contains the group name. For example,

Ribosomes, RPL3, RPL4, RPS3.

genes If entered, this parameter is a list of gene/probe identifiers corresponding to the

columns in expAll.

scale For subsets of genes that include more than one gene, this parameter determines

how the genes are combined into a single value. Currently, there are five options: 1) ("N")o scaling (default); 2) first divide each gene by the ("A")verage across samples; 3) first scale genes to ("Z")-score across samples; 4) only take the top ("H")ub gene (ignore all but the highest-connected gene); and 5) take the ("M")odule eigengene. Note that these scaling methods have not been suffi-

ciently tested, and should be considered experimental.

graph If TRUE (default), bar plot is made. If FALSE, only the results are returned, and

no plot is made.

cex1 Sets the graphing parameters of cex.axis and cex.names (default=1.5)

las1 Sets the graphing parameter las (default=2).

... Other graphing parameters allowed in the barplot function. Note that the param-

eters for cex.axis, cex.names, and las are superseded by cex1 and las1 and will

therefore be ignored.

Value

splitGroupMeans

The group/split averaged expression across each group and split combination.

This is the height of the bars in the graph.

splitGroupSDs The standard deviation of group/split expression across each group and split

combination. This is the height of the error bars in the graph.

splitPvals Kruskal-Wallis p-values for each splitting parameter across groups.

groupPvals Kruskal-Wallis p-values for each group parameter across splits.

Author(s)

Jeremy Miller

subsetTOM 397

See Also

barplot, verboseBarplot

Examples

```
# Example: first simulate some data
set.seed(100)
ME.A = sample(1:100,50); ME.B = sample(1:100,50)
ME.C = sample(1:100,50); ME.D = sample(1:100,50)
        = data.frame(ME.A, ME.B, ME.C, ME.D)
simDatA = simulateDatExpr(ME1,1000,c(0.2,0.1,0.08,0.05,0.3), signed=TRUE)
datExpr = simDatA$datExpr+5
datExpr[1:10,] = datExpr[1:10,]+2
datExpr[41:50,] = datExpr[41:50,]-1
# Now split up the data and plot it!
subset = c("Random Genes", "Gene.1", "Gene.234", "Gene.56", "Gene.789")
groups = rep(c("A", "A", "A", "B", "B", "B", "C", "C", "C", "C"), 5)
split = c(rep("ZZ",10), rep("YY",10), rep("XX",10), rep("WW",10), rep("VV",10))
par(mfrow = c(1,1))
results = stratifiedBarplot(datExpr, groups, split, subset)
results
# Now plot it the other way
results = stratifiedBarplot(datExpr, split, groups, subset)
```

subsetTOM

Topological overlap for a subset of a whole set of genes

Description

This function calculates topological overlap of a subset of vectors with respect to a whole data set.

Usage

```
subsetTOM(
  datExpr,
  subset,
  corFnc = "cor", corOptions = "use = 'p'",
  weights = NULL,
  networkType = "unsigned",
  power = 6,
  verbose = 1, indent = 0)
```

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Arguments

datExpr	a data frame containing the expression data of the whole set, with rows corresponding to samples and columns to genes.
subset	a single logical or numeric vector giving the indices of the nodes for which the TOM is to be calculated.
corFnc	character string giving the correlation function to be used for the adjacency calculation. Recommended choices are "cor" and "bicor", but other functions can be used as well.
corOptions	character string giving further options to be passed to the correlation function.
weights	optional observation weights for datExpr to be used in correlation calculation. A matrix of the same dimensions as datExpr, containing non-negative weights. Only used with Pearson correlation.
networkType	character string giving network type. Allowed values are (unique abbreviations of) "unsigned", "signed", "signed hybrid". See adjacency.
power	soft-thresholding power for network construction.
verbose	integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.
indent	indentation for diagnostic messages. Zero means no indentation, each unit adds two spaces.

Details

This function is designed to calculated topological overlaps of small subsets of large expression data sets, for example in individual modules.

Value

A matrix of dimensions n*n, where n is the number of entries selected by block.

Author(s)

Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

TOMsimilarity for standard calculation of topological overlap.

swapTwoBranches 399

swapTwoBranches Select, swap, or reflect branches in a dendrogram.	wapTwoBranches
--	----------------

Description

swapTwoBranches takes the a gene tree object and two genes as input, and swaps the branches containing these two genes at the nearest branch point of the dendrogram.

reflectBranch takes the a gene tree object and two genes as input, and reflects the branch containing the first gene at the nearest branch point of the dendrogram.

selectBranch takes the a gene tree object and two genes as input, and outputs indices for all genes in the branch containing the first gene, up to the nearest branch point of the dendrogram.

Usage

```
swapTwoBranches(hierTOM, g1, g2)
reflectBranch(hierTOM, g1, g2, both = FALSE)
selectBranch(hierTOM, g1, g2)
```

Arguments

hierTOM	A hierarchical clustering object (or gene tree) that is used to plot the dendrogram. For example, the output object from the function helust or fastcluster::hclust. Note that elements of hierTOM\$order MUST be named (for example, with the corresponding gene name).
g1	Any gene in the branch of interest.
g2	Any gene in a branch directly adjacent to the branch of interest.
both	Logical: should the selection include the branch gene g2?

Value

swapTwoBranches and reflectBranch return a hierarchical clustering object with the hierTOM\$order variable properly adjusted, but all other variables identical as the heirTOM input.

selectBranch returns a numeric vector corresponding to all genes in the requested branch.

Author(s)

Jeremy Miller

Examples

```
## Not run:
## Example: first simulate some data.
n = 30;
n2 = 2*n;
n.3 = 20;
n.5 = 10;
```

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```
MEturquoise = sample(1:(2*n),n)
MEblue = c(MEturquoise[1:(n/2)], sample(1:(2*n),n/2))
MEbrown
          = sample(1:n2,n)
MEyellow = sample(1:n2,n)
MEgreen = c(MEyellow[1:n.3], sample(1:n2,n.5))
         = c(MEbrown [1:n.5], sample(1:n2,n.3))
       = data.frame(MEturquoise, MEblue, MEbrown, MEyellow, MEgreen, MEred)
dat1 = simulateDatExpr(ME,8*n ,c(0.16,0.12,0.11,0.10,0.10,0.09,0.15),
                         signed=TRUE)
TOM1 = TOMsimilarityFromExpr(dat1$datExpr, networkType="signed")
colnames(TOM1) <- rownames(TOM1) <- colnames(dat1$datExpr)</pre>
tree1 = fastcluster::hclust(as.dist(1-TOM1),method="average")
colorh = labels2colors(dat1$allLabels)
plotDendroAndColors(tree1,colorh,dendroLabels=FALSE)
## Reassign modules using the selectBranch and chooseOneHubInEachModule functions
datExpr = dat1$datExpr
      = chooseOneHubInEachModule(datExpr, colorh)
colorh2 = rep("grey", length(colorh))
colorh2 [selectBranch(tree1,hubs["blue"],hubs["turquoise"])] = "blue"
colorh2 [selectBranch(tree1,hubs["turquoise"],hubs["blue"])] = "turquoise"
colorh2 [selectBranch(tree1,hubs["green"],hubs["yellow"])] = "green"
colorh2 [selectBranch(tree1,hubs["yellow"],hubs["green"])] = "yellow"
colorh2 [selectBranch(tree1, hubs["red"], hubs["brown"])]
colorh2 [selectBranch(tree1,hubs["brown"],hubs["red"])]
plotDendroAndColors(tree1,cbind(colorh,colorh2),c("Old","New"),dendroLabels=FALSE)
## Now swap and reflect some branches, then optimize the order of the branches
# Open a suitably sized graphics window
sizeGrWindow(12,9);
# partition the screen for 3 dendrogram + module color plots
layout(matrix(c(1:6), 6, 1), heights = c(0.8, 0.2, 0.8, 0.2, 0.8, 0.2));
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Starting Dendrogram",
                    setLayout = FALSE)
tree1 = swapTwoBranches(tree1,hubs["red"],hubs["turquoise"])
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Swap blue/turquoise and red/brown",
                    setLayout = FALSE)
tree1 = reflectBranch(tree1,hubs["blue"],hubs["green"])
plotDendroAndColors(tree1,colorh2,dendroLabels=FALSE,main="Reflect turquoise/blue",
                    setLayout = FALSE)
## End(Not run)
```

TOMplot 401

TOMplot	Graphical representation of the Topological Overlap Matrix

Description

Graphical representation of the Topological Overlap Matrix using a heatmap plot combined with the corresponding hierarchical clustering dendrogram and module colors.

Usage

```
TOMplot(
    dissim,
    dendro,
    Colors = NULL,
    ColorsLeft = Colors,
    terrainColors = FALSE,
    setLayout = TRUE,
    ...)
```

Arguments

dissim	a matrix containing the topological overlap-based dissimilarity
dendro	the corresponding hierarchical clustering dendrogram
Colors	optional specification of module colors to be plotted on top
ColorsLeft	optional specification of module colors on the left side. If NULL, Colors will be used. $ \\$
terrainColors	logical: should terrain colors be used?
setLayout	logical: should layout be set? If TRUE, standard layout for one plot will be used. Note that this precludes multiple plots on one page. If FALSE, the user is responsible for setting the correct layout.
	other graphical parameters to heatmap.

Details

The standard heatmap function uses the layout function to set the following layout (when Colors is given):

```
0 0 5
0 0 2
4 1 3
```

To get a meaningful heatmap plot, user-set layout must respect this geometry.

Value

None.

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Author(s)

Steve Horvath and Peter Langfelder

See Also

heatmap, the workhorse function doing the plotting.

TOMsimilarity

Topological overlap matrix similarity and dissimilarity

Description

Calculation of the topological overlap matrix, and the corresponding dissimilarity, from a given adjacency matrix.

Usage

```
TOMsimilarity(
    adiMat,
    TOMType = "unsigned",
    TOMDenom = "min",
    suppressTOMForZeroAdjacencies = FALSE,
    suppressNegativeTOM = FALSE,
    useInternalMatrixAlgebra = FALSE,
    verbose = 1,
    indent = 0)
TOMdist(
    adjMat,
    TOMType = "unsigned",
    TOMDenom = "min",
    suppressTOMForZeroAdjacencies = FALSE,
    suppressNegativeTOM = FALSE,
    useInternalMatrixAlgebra = FALSE,
    verbose = 1,
    indent = 0)
```

Arguments

adjacency matrix, that is a square, symmetric matrix with entries between 0 and

1 (negative values are allowed if TOMType=="signed").

TOMType one of "none", "unsigned", "signed Nowick", "unsigned 2", "signed

2" and "signed Nowick 2". If "none", adjacency will be used for clustering.

See TOMsimilarityFromExpr for details.

TOMDenom a character string specifying the TOM variant to be used. Recognized values

are "min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean.

TOMsimilarity 403

The "mean" may produce better results but at this time should be considered experimental.

suppressTOMForZeroAdjacencies

Logical: should the results be set to zero for zero adjacencies?

suppressNegativeTOM

Logical: should the result be set to zero when negative?

useInternalMatrixAlgebra

Logical: should WGCNA's own, slow, matrix multiplication be used instead of

R-wide BLAS? Only useful for debugging.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

The functions perform basically the same calculations of topological overlap. TOMdist turns the overlap (which is a measure of similarity) into a measure of dissimilarity by subtracting it from 1.

Basic checks on the adjacency matrix are performed and missing entries are replaced by zeros.

See TOMsimilarityFromExpr for details on the various TOM types.

The underlying C code assumes that the diagonal of the adjacency matrix equals 1. If this is not the case, the diagonal of the input is set to 1 before the calculation begins.

Value

A matrix holding the topological overlap.

Author(s)

Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

For the Nowick-type signed TOM (referred to as weighted TO, wTO, by Nowick et al.), see

Nowick K, Gernat T, Almaas E, Stubbs L. Differences in human and chimpanzee gene expression patterns define an evolving network of transcription factors in brain. Proc Natl Acad Sci U S A. 2009 Dec 29;106(52):22358-63. doi: 10.1073/pnas.0911376106. Epub 2009 Dec 10.

or Gysi DM, Voigt A, Fragoso TM, Almaas E, Nowick K. wTO: an R package for computing weighted topological overlap and a consensus network with integrated visualization tool. BMC Bioinformatics. 2018 Oct 24;19(1):392. doi: 10.1186/s12859-018-2351-7.

See Also

TOMsimilarityFromExpr

TOMsimilarityFromExpr Topological overlap matrix

Description

Calculation of the topological overlap matrix from given expression data.

Usage

```
TOMsimilarityFromExpr(
  datExpr,
 weights = NULL,
  corType = "pearson",
  networkType = "unsigned",
  power = 6,
  TOMType = "signed",
  TOMDenom = "min",
 maxPOutliers = 1,
 quickCor = 0,
  pearsonFallback = "individual",
  cosineCorrelation = FALSE,
  replaceMissingAdjacencies = FALSE,
  suppressTOMForZeroAdjacencies = FALSE,
  suppressNegativeTOM = FALSE,
  useInternalMatrixAlgebra = FALSE,
  nThreads = 0,
  verbose = 1, indent = 0)
```

Arguments

datExpr expression data. A data frame in which columns are genes and rows ar samples.

NAs are allowed, but not too many.

weights optional observation weights for datExpr to be used in correlation calculation.

A matrix of the same dimensions as datExpr, containing non-negative weights.

corType character string specifying the correlation to be used. Allowed values are (unique

abbreviations of) "pearson" and "bicor", corresponding to Pearson and bid-

weight midcorrelation, respectively. Missing values are handled using the pairwise.complete.obs

option.

networkType network type. Allowed values are (unique abbreviations of) "unsigned", "signed",

"signed hybrid". See adjacency.

power soft-thresholding power for netwoek construction.

TOMType one of "none", "unsigned", "signed Nowick", "unsigned 2", "signed

2" and "signed Nowick 2". If "none", adjacency will be used for clustering. See details and keep in mind that the "2" versions should be considered experi-

mental and are subject to change.

TOMDenom

a character string specifying the TOM variant to be used. Recognized values are "min" giving the standard TOM described in Zhang and Horvath (2005), and "mean" in which the min function in the denominator is replaced by mean. The "mean" may produce better results but at this time should be considered experimental.

maxPOutliers

only used for corType=="bicor". Specifies the maximum percentile of data that can be considered outliers on either side of the median separately. For each side of the median, if higher percentile than maxPOutliers is considered an outlier by the weight function based on 9*mad(x), the width of the weight function is increased such that the percentile of outliers on that side of the median equals maxPOutliers. Using maxPOutliers=1 will effectively disable all weight function broadening; using maxPOutliers=0 will give results that are quite similar (but not equal to) Pearson correlation.

quickCor

real number between 0 and 1 that controls the handling of missing data in the calculation of correlations. See details.

pearsonFallback

Specifies whether the bicor calculation, if used, should revert to Pearson when median absolute deviation (mad) is zero. Recongnized values are (abbreviations of) "none", "individual", "all". If set to "none", zero mad will result in NA for the corresponding correlation. If set to "individual", Pearson calculation will be used only for columns that have zero mad. If set to "all", the presence of a single zero mad will cause the whole variable to be treated in Pearson correlation manner (as if the corresponding robust option was set to FALSE). Has no effect for Pearson correlation. See bicor.

cosineCorrelation

logical: should the cosine version of the correlation calculation be used? The cosine calculation differs from the standard one in that it does not subtract the mean.

replaceMissingAdjacencies

logical: should missing values in the calculation of adjacency be replaced by 0? suppressTOMForZeroAdjacencies

Logical: should the result be set to zero for zero adjacencies?

suppressNegativeTOM

Logical: should the result be set to zero when negative?

useInternalMatrixAlgebra

Logical: should WGCNA's own, slow, matrix multiplication be used instead of R-wide BLAS? Only useful for debugging.

nThreads

non-negative integer specifying the number of parallel threads to be used by certain parts of correlation calculations. This option only has an effect on systems on which a POSIX thread library is available (which currently includes Linux and Mac OSX, but excludes Windows). If zero, the number of online processors will be used if it can be determined dynamically, otherwise correlation calculations will use 2 threads.

verbose

integer level of verbosity. Zero means silent, higher values make the output progressively more and more verbose.

indent

indentation for diagnostic messages. Zero means no indentation, each unit adds two spaces.

Details

Several alternate definitions of topological overlap are available. The oldest version is now called "unsigned"; in this version, all adjacencies are assumed to be non-negative and the topological overlap of nodes i, j is given by

$$TOM_{ij} = \frac{a_{ij} + \sum_{k \neq i,j} a_{ik} a_{kj}}{f(k_i, k_j) + 1 - a_{ij}},$$

where the sum is over k not equal to either i or j, the function f in the denominator can be either min or mean (goverened by argument TOMDenom), and $k_i = \sum_{j \neq i} a_{ij}$ is the connectivity of node i. The signed versions assume that the adjacency matrix was obtained from an underlying correlation matrix, and the element a_{ij} carries the sign of the underlying correlation of the two vectors. (Within WGCNA, this can really only apply to the unsigned adjacency since signed adjacencies are (essentially) zero when the underlying correlation is negative.) The signed and signed Nowick versions are similar to the above unsigned version, differing only in absolute values placed in the expression: the signed Nowick expression is

$$TOM_{ij} = \frac{a_{ij} + \sum_{k \neq i,j} a_{ik} a_{kj}}{f(k_i, k_j) + 1 - |a_{ij}|}.$$

This TOM lies between -1 and 1, and typically is negative when the underlying adjacency is negative. The signed TOM is simply the absolute value of the signed Nowick TOM and is hence always non-negative. For non-negative adjacencies, all 3 version give the same result.

A brief note on terminology: the original article by Nowick et al use the name "weighted TO" or wTO; since all of the topological overlap versions calculated in this function are weighted, we use the name signed to indicate that this TOM keeps track of the sign of the underlying correlation.

The "2" versions of all 3 adjacency types have a somewhat different form in which the adjacency and the product are normalized separately. Thus, the "unsigned 2" version is

$$TOM_{ij}^{(2)} = \frac{1}{2} \left[a_{ij} + \frac{\sum_{k \neq i,j} a_{ik} a_{kj}}{f(k_i, k_j) - a_{ij}} \right].$$

At present the relative weight of the adjacency and the normalized product term are equal and fixed; in the future a user-specified or automatically determined weight may be implemented. The "signed Nowick 2" and "signed 2" are defined analogously to their original versions. The adjacency is assumed to be signed, and the expression for "signed Nowick 2" TOM is

$$TOM_{ij}^{(2)} = \frac{1}{2} \left[a_{ij} + \frac{\sum_{k \neq i,j} a_{ik} a_{kj}}{f(k_i, k_j) - |a_{ij}|} \right].$$

Analogously to "signed" TOM, "signed 2" differs from "signed Nowick 2" TOM only in taking the absolute value of the result.

At present the "2" versions should all be considered experimental and are subject to change.

Value

A matrix holding the topological overlap.

transposeBigData 407

Author(s)

Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

TOMsimilarity

transposeBigData

Transpose a big matrix or data frame

Description

This transpose command partitions a big matrix (or data frame) into blocks and applies the t() function to each block separately.

Usage

```
transposeBigData(x, blocksize = 20000)
```

Arguments

x a matrix or data frame

blocksize a positive integer larger than 1, which determines the block size. Default is 20k.

Details

Assume you have a very large matrix with say 500k columns. In this case, the standard transpose function of R t() can take a long time. Solution: Split the original matrix into sub-matrices by dividing the columns into blocks. Next apply t() to each sub-matrix. The same holds if the large matrix contains a large number of rows. The function transposeBigData automatically checks whether the large matrix contains more rows or more columns. If the number of columns is larger than or equal to the number of rows then the block wise splitting will be applied to columns otherwise to the rows.

Value

A matrix or data frame (depending on the input x) which is the transpose of x.

Note

This function can be considered a wrapper of t()

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Author(s)

Steve Horvath, UCLA

References

Any linear algebra book will explain the transpose.

See Also

The standard function t.

Examples

```
x=data.frame(matrix(1:10000,nrow=4,ncol=2500))
dimnames(x)[[2]]=paste("Y",1:2500,sep="")
xTranspose=transposeBigData(x)
x[1:4,1:4]
xTranspose[1:4,1:4]
```

TrueTrait

Estimate the true trait underlying a list of surrogate markers.

Description

Assume an imprecisely measured trait y that is related to the true, unobserved trait yTRUE as follows yTRUE=y+noise where noise is assumed to have mean zero and a constant variance. Assume you have 1 or more surrogate markers for yTRUE corresponding to the columns of datX. The function implements several approaches for estimating yTRUE based on the inputs y and/or datX.

Usage

Arguments

datX is a vector or data frame whose columns correspond to the surrogate markers

(variables) for the true underlying trait. The number of rows of datX equals the

number of observations, i.e. it should equal the length of y

y is a numeric vector which specifies the observed trait.

datXtest can be set as a matrix or data frame of a second, independent test data set. Its

columns should correspond to those of datX, i.e. the two data sets should have the same number of columns but the number or rows (test set observations) can

be different.

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corFnc Character string specifying the correlation function to be used in the calcula-

tions. Recomended values are the default Pearson correlation "cor" or biweight mid-correlation "bicor". Additional arguments to the correlation function can

be specified using corOptions.

corOptions Character string giving additional arguments to the function specified in corFnc.

LeaveOneOut.CV logical. If TRUE then leave one out cross validation estimates will be calculated

for y.true1 and y.true2 based on datX.

skipMissingVariables

logical. If TRUE then variables whose values are missing for a given observation will be skipped when estimating the true trait of that particular observation. Thus, the estimate of a particular observation are determined by all the variables whose values are non missing.

whose values are non-missing.

addLinearModel logical. If TRUE then the function also estimates the true trait based on the

predictions of the linear model $lm(y^{-}., data=datX)$

Details

This R function implements formulas described in Klemera and Doubal (2006). The assumptions underlying these formulas are described in Klemera et al. But briefly, the function provides several estimates of the true underlying trait under the following assumptions: 1) There is a true underlying trait that affects y and a list of surrogate markers corresponding to the columns of datX. 2) There is a linear relationship between the true underlying trait and y and the surrogate markers. 3) yTRUE =y +Noise where the Noise term has a mean of zero and a fixed variance. 4) Weighted least squares estimation is used to relate the surrogate markers to the underlying trait where the weights are proportional to 1/ssq.j where ssq.j is the noise variance of the j-th marker.

Specifically, output y.true1 corresponds to formula 31, y.true2 corresponds to formula 25, and y.true3 corresponds to formula 34.

Although the true underlying trait yTRUE is not known, one can estimate the standard deviation between the estimate y.true2 and yTRUE using formula 33. Similarly, one can estimate the SD for the estimate y.true3 using formula 42. These estimated SDs correspond to output components 2 and 3, respectively. These SDs are valuable since they provide a sense of how accurate the measure is

To estimate the correlations between y and the surrogate markers, one can specify different correlation measures. The default method is based on the Person correlation but one can also specify the biweight midcorrelation by choosing "bicor", see help(bicor) to learn more.

When the datX is comprised of observations measured in different strata (e.g. different batches or independent data sets) then one can obtain stratum specific estimates by specifying the strata using the argument Strata. In this case, the estimation focuses on one stratum at a time.

Value

A list with the following components.

datEstimates

is a data frame whose columns corresponds to estimates of the true underlying trait. The number of rows equals the number of observations, i.e. the length of y. The first column y.true1 is the average value of standardized columns of datX where standardization subtracts out the intercept term and divides by the slope

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of the linear regression model lm(marker~y). Since this estimate ignores the fact that the surrogate markers have different correlations with y, it is typically inferior to y.true2. The second column y.true2 equals the weighted average value of standardized columns of datX. The standardization is described in section 2.4 of Klemera et al. The weights are proportional to r^2/(1+r^2) where r denotes the correlation between the surrogate marker and y. Since this estimate does not include y as additional surrogate marker, it may be slightly inferior to y.true3. Having said this, the difference between y.true2 and y.true3 is often negligible. An additional column called y.lm is added if addLinearModel=TRUE. In this case, y.lm reports the linear model predictions. Finally, the column y.true3 is very similar to y.true2 but it includes y as additional surrogate marker. It is expected to be the best estimate of the underlying true trait (see Klemera et al 2006).

datEstimatestest

is output only if a test data set has been specified in the argument datXtest. In this case, it contains a data frame with columns ytrue1 and ytrue2. The number of rows equals the number of test set observations, i.e the number of rows of datXtest. Since the value of y is not known in case of a test data set, one cannot calculate y.true3. An additional column with linear model predictions y.lm is added if addLinearModel=TRUE.

datEstimates.LeaveOneOut.CV

is output only if the argument LeaveOneOut.CV has been set to TRUE. In this case, it contains a data frame with leave-one-out cross validation estimates of ytrue1 and ytrue2. The number of rows equals the length of y. Since the value of y is not known in case of a test data set, one cannot calculate y.true3

SD.ytrue2

is a scalar. This is an estimate of the standard deviation between the estimate y.true2 and the true (unobserved) yTRUE. It corresponds to formula 33.

SD.ytrue3

is a scalar. This is an estimate of the standard deviation between y.true3 and the true (unobserved) yTRUE. It corresponds to formula 42.

datVariableInfo

is a data frame that reports information for each variable (column of datX) when it comes to the definition of y.true2. The rows correspond to the number of variables. Columns report the variable name, the center (intercept that is subtracted to scale each variable), the scale (i.e. the slope that is used in the denominator), and finally the weights used in the weighted sum of the scaled variables.

datEstimatesByStratum

a data frame that will only be output if Strata is different from NULL. In this case, it is has the same dimensions as datEstimates but the estimates were calculated separately for each level of Strata.

SD.ytrue2ByStratum

a vector of length equal to the different levels of Strata. Each component reports the estimate of SD.ytrue2 for observations in the stratum specified by unique(Strata).

datVariableInfoByStratum

a list whose components are matrices with variable information. Each list component reports the variable information in the stratum specified by unique(Strata).

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Author(s)

Steve Horvath

References

Klemera P, Doubal S (2006) A new approach to the concept and computation of biological age. Mechanisms of Ageing and Development 127 (2006) 240-248

Choa IH, Parka KS, Limb CJ (2010) An Empirical Comparative Study on Validation of Biological Age Estimation Algorithms with an Application of Work Ability Index. Mechanisms of Ageing and Development Volume 131, Issue 2, February 2010, Pages 69-78

Examples

```
# observed trait
y=rnorm(1000, mean=50, sd=20)
# unobserved, true trait
yTRUE =y +rnorm(100, sd=10)
# now we simulate surrogate markers around the true trait
datX=simulateModule(yTRUE,nGenes=20, minCor=.4,maxCor=.9,geneMeans=rnorm(20,50,30) )
True1=TrueTrait(datX=datX,y=y)
datTrue=True1$datEstimates
par(mfrow=c(2,2))
for (i in 1:dim(datTrue)[[2]] ){
  meanAbsDev= mean(abs(yTRUE-datTrue[,i]))
  verboseScatterplot(datTrue[,i],yTRUE,xlab=names(datTrue)[i],
                     main=paste(i, "MeanAbsDev=", signif(meanAbsDev,3)));
  abline(0,1)
}
#compare the estimated standard deviation of y.true2
True1[[2]]
# with the true SD
sqrt(var(yTRUE-datTrue$y.true2))
#compare the estimated standard deviation of y.true3
True1[[3]]
# with the true SD
sqrt(var(yTRUE-datTrue$y.true3))
```

unsignedAdjacency

Calculation of unsigned adjacency

Description

Calculation of the unsigned network adjacency from expression data. The restricted set of parameters for this function should allow a faster and less memory-hungry calculation.

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Usage

```
unsignedAdjacency(
  datExpr,
  datExpr2 = NULL,
  power = 6,
  corFnc = "cor", corOptions = "use = 'p'")
```

Arguments

datExpr expression data. A data frame in which columns are genes and rows ar samples.

Missing values are ignored.

datExpr2 optional specification of a second set of expression data. See details.

power soft-thresholding power for network construction.

corFnc character string giving the correlation function to be used for the adjacency cal-

culation. Recommended choices are "cor" and "bicor", but other functions

can be used as well.

corOptions character string giving further options to be passed to the correlation function

Details

The correlation function will be called with arguments datExpr, datExpr2 plus any extra arguments given in corOptions. If datExpr2 is NULL, the standard correlation functions will calculate the corelation of columns in datExpr.

Value

Adjacency matrix of dimensions n*n, where n is the number of genes in datExpr.

Author(s)

Steve Horvath and Peter Langfelder

References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

adjacency

userListEnrichment

Measure enrichment between inputted and user-defined lists

Description

This function measures list enrichment between inputted lists of genes and files containing user-defined lists of genes. Significant enrichment is measured using a hypergeometric test. A pre-made collection of brain-related lists can also be loaded. The function writes the significant enrichments to a file, but also returns all overlapping genes across all comparisons.

Usage

```
userListEnrichment(
  geneR, labelR,
  fnIn = NULL, catNmIn = fnIn,
  nameOut = "enrichment.csv",
  useBrainLists = FALSE, useBloodAtlases = FALSE, omitCategories = "grey",
  outputCorrectedPvalues = TRUE, useStemCellLists = FALSE,
  outputGenes = FALSE,
  minGenesInCategory = 1,
  useBrainRegionMarkers = FALSE, useImmunePathwayLists = FALSE,
  usePalazzoloWang = FALSE)
```

Arguments

geneR	A vector of gene (or other) identifiers. This vector should include ALL genes in your analysis (i.e., the genes correspoding to your labeled lists AND the remaining background reference genes).
labelR	A vector of labels (for example, module assignments) corresponding to the geneR list. NOTE: For all background reference genes that have no corresponding label, use the label "background" (or any label included in the omitCategories parameter).
fnIn	A vector of file names containing user-defined lists. These files must be in one of three specific formats (see details section). The default (NULL) may only be used if one of the "use" parameters is TRUE.
catNmIn	A vector of category names corresponding to each fnIn. This name will be appended to each overlap corresponding to that filename. The default sets the category names as the corresponding file names.
nameOut	Name of the file where the output enrichment information will be written. (Note that this file includes only a subset of what is returned by the function.) If NULL (or zero-length), no output will be written out.
useBrainLists	If TRUE, a pre-made set of brain-derived enrichment lists will be added to any user-defined lists for enrichment comparison. The default is FALSE. See references section for related references.

useBloodAtlases

If TRUE, a pre-made set of blood-derived enrichment lists will be added to any user-defined lists for enrichment comparison. The default is FALSE. See references section for related references.

omitCategories Any labelR entries corresponding to these categories will be ignored. The default ("grey") will ignore unassigned genes in a standard WGCNA network.

outputCorrectedPvalues

If TRUE (default) only pvalues that are significant after correcting for multiple comparisons (using Bonferroni method) will be outputted to nameOut. Otherwise the uncorrected p-values will be outputted to the file. Note that both sets of p-values for all comparisons are reported in the returned "pValues" parameter.

useStemCellLists

If TRUE, a pre-made set of stem cell (SC)-derived enrichment lists will be added to any user-defined lists for enrichment comparison. The default is FALSE. See references section for related references.

outputGenes

If TRUE, will output a list of all genes in each returned category, as well as a count of the number of genes in each category. The default is FALSE.

minGenesInCategory

Will omit all significant categories with fewer than minGenesInCategory genes (default is 1).

useBrainRegionMarkers

If TRUE, a pre-made set of enrichment lists for human brain regions will be added to any user-defined lists for enrichment comparison. The default is FALSE. These lists are derived from data from the Allen Human Brain Atlas (https://human.brainmap.org/). See references section for more details.

useImmunePathwayLists

If TRUE, a pre-made set of enrichment lists for immune system pathways will be added to any user-defined lists for enrichment comparison. The default is FALSE. These lists are derived from the lab of Daniel R Saloman. See references section for more details.

usePalazzoloWang

If TRUE, a pre-made set of enrichment lists compiled by Mike Palazzolo and Jim Wang from CHDI will be added to any user-defined lists for enrichment comparison. The default is FALSE. See references section for more details.

Details

User-inputted files for fnIn can be in one of three formats:

- 1) Text files (must end in ".txt") with one list per file, where the first line is the list descriptor and the remaining lines are gene names corresponding to that list, with one gene per line. For example Ribosome RPS4 RPS8 ...
- 2) Gene / category files (must be csv files), where the first line is the column headers corresponding to Genes and Lists, and the remaining lines correspond to the genes in each list, for any number of genes and lists. For example: Gene, Category RPS4, Ribosome RPS8, Ribosome ... NDUF1, Mitohcondria NDUF3, Mitochondria ... MAPT, AlzheimersDisease PSEN1, AlzheimersDisease PSEN2, AlzheimersDisease ...

3) Module membership (kME) table in csv format. Currently, the module assignment is the only thing that is used, so as long as the Gene column is 2nd and the Module column is 3rd, it doesn't matter what is in the other columns. For example, PSID, Gene, Module, <other columns> <psid>, RPS4, blue, <other columns> <psid>, NDUF1, red, <other columns> <psid>, RPS8, blue, <other columns> <psid>, NDUF3, red, <other columns> <psid>, MAPT, green, <other columns> ...

Value

pValues A data frame showing, for each comparison, the input category, user defined

category, type, the number of overlapping genes and both the uncorrected and

Bonferroni corrected p-values for every pair of list overlaps tested.

ovGenes A list of character vectors corresponding to the overlapping genes for every

pair of list overlaps tested. Specific overlaps can be found by typing <variable-Name>\$ovGenes\$'<labelR> - <comparisonCategory>'. See example below.

sigOverlaps Identical information that is written to nameOut. A data frame ith columns giv-

ing the input category, user defined category, type, and P-values (corrected or uncorrected, depending on outputCorrectedPvalues) corresponding to all signif-

icant enrichments.

Author(s)

Jeremy Miller

References

The primary reference for this function is: Miller JA, Cai C, Langfelder P, Geschwind DH, Kurian SM, Salomon DR, Horvath S. (2011) Strategies for aggregating gene expression data: the collapseRows R function. BMC Bioinformatics 12:322.

If you have any suggestions for lists to add to this function, please e-mail Jeremy Miller at jere-myinla@gmail.com

ABA ==> Cell type markers from: Lein ES, et al. (2007) Genome-wide atlas of gene expression in the adult mouse brain. Nature 445:168-176.

ADvsCT_inCA1 ==> Lists of genes found to be increasing or decreasing with Alzheimer's disease in 3 studies: 1. Blalock => Blalock E, Geddes J, Chen K, Porter N, Markesbery W, Landfield P (2004) Incipient Alzheimer's disease: microarray correlation analyses reveal major transcriptional and tumor suppressor responses. PNAS 101:2173-2178. 2. Colangelo => Colangelo V, Schurr J, Ball M, Pelaez R, Bazan N, Lukiw W (2002) Gene expression profiling of 12633 genes in Alzheimer hippocampal CA1: transcription and neurotrophic factor down-regulation and upregulation of apoptotic and pro-inflammatory signaling. J Neurosci Res 70:462-473. 3. Liang => Liang WS, et al (2008) Altered neuronal gene expression in brain regions differentially affected by Alzheimer's disease: a reference data set. Physiological genomics 33:240-56.

Bayes ==> Postsynaptic Density Proteins from: Bayes A, et al. (2011) Characterization of the proteome, diseases and evolution of the human postsynaptic density. Nat Neurosci. 14(1):19-21.

Blalock_AD ==> Modules from a network using the data from: Blalock E, Geddes J, Chen K, Porter N, Markesbery W, Landfield P (2004) Incipient Alzheimer's disease: microarray correlation analyses reveal major transcriptional and tumor suppressor responses. PNAS 101:2173-2178.

CA1vsCA3 ==> Lists of genes enriched in CA1 and CA3 relative to other each and to other areas of the brain, from several studies: 1. Ginsberg => Ginsberg SD, Che S (2005) Expression profile analysis within the human hippocampus: comparison of CA1 and CA3 pyramidal neurons. J Comp Neurol 487:107-118. 2. Lein => Lein E, Zhao X, Gage F (2004) Defining a molecular atlas of the hippocampus using DNA microarrays and high-throughput in situ hybridization. J Neurosci 24:3879-3889. 3. Newrzella => Newrzella D, et al (2007) The functional genome of CA1 and CA3 neurons under native conditions and in response to ischemia. BMC Genomics 8:370. 4. Torres => Torres-Munoz JE, Van Waveren C, Keegan MG, Bookman RJ, Petito CK (2004) Gene expression profiles in microdissected neurons from human hippocampal subregions. Brain Res Mol Brain Res 127:105-114. 5. GorLorT => In either Ginsberg or Lein or Torres list.

Cahoy ==> Definite (10+ fold) and probable (1.5+ fold) enrichment from: Cahoy JD, et al. (2008) A transcriptome database for astrocytes, neurons, and oligodendrocytes: A new resource for understanding brain development and function. J Neurosci 28:264-278.

CTX ==> Modules from the CTX (cortex) network from: Oldham MC, et al. (2008) Functional organization of the transcriptome in human brain. Nat Neurosci 11:1271-1282.

DiseaseGenes ==> Probable (C or better rating as of 16 Mar 2011) and possible (all genes in database as of ~2008) genetics-based disease genes from: http://www.alzforum.org/

EarlyAD ==> Genes whose expression is related to cognitive markers of early Alzheimer's disease vs. non-demented controls with AD pathology, from: Parachikova, A., et al (2007) Inflammatory changes parallel the early stages of Alzheimer disease. Neurobiology of Aging 28:1821-1833.

HumanChimp ==> Modules showing region-specificity in both human and chimp from: Oldham MC, Horvath S, Geschwind DH (2006) Conservation and evolution of gene coexpression networks in human and chimpanzee brains. Proc Natl Acad Sci USA 103: 17973-17978.

HumanMeta ==> Modules from the human network from: Miller J, Horvath S, Geschwind D (2010) Divergence of human and mouse brain transcriptome highlights Alzheimer disease pathways. Proc Natl Acad Sci 107:12698-12703.

JAXdiseaseGene ==> Genes where mutations in mouse and/or human are known to cause any disease. WARNING: this list represents an oversimplification of data! This list was created from the Jackson Laboratory: Bult CJ, Eppig JT, Kadin JA, Richardson JE, Blake JA; Mouse Genome Database Group (2008) The Mouse Genome Database (MGD): Mouse biology and model systems. Nucleic Acids Res 36 (database issue):D724-D728.

Lu_Aging ==> Modules from a network using the data from: Lu T, Pan Y, Kao S-Y, Li C, Kohane I, Chan J, Yankner B (2004) Gene regulation and DNA damage in the ageing human brain. Nature 429:883-891.

MicroglialMarkers ==> Markers for microglia and macrophages from several studies: 1. GSE772 => Gan L, et al. (2004) Identification of cathepsin B as a mediator of neuronal death induced by Abeta-activated microglial cells using a functional genomics approach. J Biol Chem 279:5565-5572. 2. GSE1910 => Albright AV, Gonzalez-Scarano F (2004) Microarray analysis of activated mixed glial (microglia) and monocyte-derived macrophage gene expression. J Neuroimmunol 157:27-38. 3. AitGhezala => Ait-Ghezala G, Mathura VS, Laporte V, Quadros A, Paris D, Patel N, et al. Genomic regulation after CD40 stimulation in microglia: relevance to Alzheimer's disease. Brain Res Mol Brain Res 2005;140(1-2):73-85. 4. 3treatments_Thomas => Thomas, DM,

Francescutti-Verbeem, DM, Kuhn, DM (2006) Gene expression profile of activated microglia under conditions associated with dopamine neuronal damage. The FASEB Journal 20:515-517.

MitochondrialType ==> Mitochondrial genes from the somatic vs. synaptic fraction of mouse cells from: Winden KD, et al. (2009) The organization of the transcriptional network in specific neuronal classes. Mol Syst Biol 5:291.

MO ==> Markers for many different things provided to my by Mike Oldham. These were originally from several sources: 1. 2+_26Mar08 => Genetics-based disease genes in two or more studies from http://www.alzforum.org/ (compiled by Mike Oldham). 2. Bachoo => Bachoo, R.M. et al. (2004) Molecular diversity of astrocytes with implications for neurological disorders. PNAS 101, 8384-8389. 3. Foster => Foster, LJ, de Hoog, CL, Zhang, Y, Zhang, Y, Xie, X, Mootha, VK, Mann, M. (2006) A Mammalian Organelle Map by Protein Correlation Profiling. Cell 125(1): 187-199. 4. Morciano => Morciano, M. et al. Immunoisolation of two synaptic vesicle pools from synaptosomes: a proteomics analysis. J. Neurochem. 95, 1732-1745 (2005). 5. Sugino => Sugino, K. et al. Molecular taxonomy of major neuronal classes in the adult mouse forebrain. Nat. Neurosci. 9, 99-107 (2006).

MouseMeta ==> Modules from the mouse network from: Miller J, Horvath S, Geschwind D (2010) Divergence of human and mouse brain transcriptome highlights Alzheimer disease pathways. Proc Natl Acad Sci 107:12698-12703.

Sugino/Winden ==> Conservative list of genes in modules from the network from: Winden K, Oldham M, Mirnics K, Ebert P, Swan C, Levitt P, Rubenstein J, Horvath S, Geschwind D (2009). The organization of the transcriptional network in specific neuronal classes. Molecular systems biology 5. NOTE: Original data came from this neuronal-cell-type-selection experiment in mouse: Sugino K, Hempel C, Miller M, Hattox A, Shapiro P, Wu C, Huang J, Nelson S (2006). Molecular taxonomy of major neuronal classes in the adult mouse forebrain. Nat Neurosci 9:99-107

Voineagu ==> Several Autism-related gene categories from: Voineagu I, Wang X, Johnston P, Lowe JK, Tian Y, Horvath S, Mill J, Cantor RM, Blencowe BJ, Geschwind DH. (2011). Transcriptomic analysis of autistic brain reveals convergent molecular pathology. Nature 474(7351):380-4

Blood(composite) ==> Lists for blood cell types with this label are made from combining marker genes from the following three publications: 1. Abbas AB, Baldwin D, Ma Y, Ouyang W, Gurney A, et al. (2005). Immune response in silico (IRIS): immune-specific genes identified from a compendium of microarray expression data. Genes Immun. 6(4):319-31. 2. Grigoryev YA, Kurian SM, Avnur Z, Borie D, Deng J, et al. (2010). Deconvoluting post-transplant immunity: cell subset-specific mapping reveals pathways for activation and expansion of memory T, monocytes and B cells. PLoS One. 5(10):e13358. 3. Watkins NA, Gusnanto A, de Bono B, De S, Miranda-Saavedra D, et al. (2009). A HaemAtlas: characterizing gene expression in differentiated human blood cells. Blood. 113(19):e1-9.

Gnatenko ==> Top 50 marker genes for platelets from: Gnatenko DV, et al. (2009) Transcript profiling of human platelets using microarray and serial analysis of gene expression (SAGE). Methods Mol Biol. 496:245-72.

Gnatenko2 ==> Platelet-specific genes on a custom microarray from: Gnatenko DV, et al. (2010) Class prediction models of thrombocytosis using genetic biomarkers. Blood. 115(1):7-14.

Kabanova ==> Red blood cell markers from: Kabanova S, et al. (2009) Gene expression analysis of human red blood cells. Int J Med Sci. 6(4):156-9.

Whitney ==> Genes corresponding to individual variation in blood from: Whitney AR, et al. (2003) Individuality and variation in gene expression patterns in human blood. PNAS. 100(4):1896-1901.

Cui ==> genes differentiating erythrocyte precursors (CD36+ cells) from multipotent human primary hematopoietic stem cells/progenitor cells (CD133+ cells), from: Cui K, Zang C, Roh TY, Schones DE, Childs RW, Peng W, Zhao K. (2009). Chromatin signatures in multipotent human hematopoietic stem cells indicate the fate of bivalent genes during differentiation. Cell Stem Cell 4:80-93

Lee ==> gene lists related to Polycomb proteins in human embryonic SCs, from (a highly-cited paper!): Lee TI, Jenner RG, Boyer LA, Guenther MG, Levine SS, Kumar RM, Chevalier B, Johnstone SE, Cole MF, Isono K, et al. (2006) Control of developmental regulators by polycomb in human embryonic stem cells. Cell 125:301-313

HBA ==> Hawrylycz MJ, Lein ES, Guillozet-Bongaarts AL, Shen EH, Ng L, Miller JA, et al. (2012) An Anatomically Comprehensive Atlas of the Adult Human Brain Transcriptome. Nature (in press) Three categories of marker genes are presented: 1. globalMarker(top200) = top 200 global marker genes for 22 large brain structures. Genes are ranked based on fold change enrichment (expression in region vs. expression in rest of brain) and the ranks are averaged between brains 2001 and 2002 (human.brain-map.org). 2. localMarker(top200) = top 200 local marker genes for 90 large brain structures. Same as 1, except fold change is defined as expression in region vs. expression in larger region (format: <region>_IN_<largerRegion>). For example, enrichment in CA1 is relative to other subcompartments of the hippocampus. 3. localMarker(FC>2) = same as #2, but only local marker genes with fold change > 2 in both brains are included. Regions with <10 marker genes are omitted.

ImmunePathway ==> These lists were created by Brian Modena (a member of Daniel R Salomon's lab at Scripps Research Institute), with input from Sunil M Kurian and Dr. Salomon, using Ingenuity, WikiPathways and literature search to assemble them. They reflect knowledge-based immune pathways and were in part informed by Dr. Salomon and colleague's work in expression profiling of biopsies and peripheral blood but not in some highly organized process. These lists are not from any particular publication, but are culled to include only genes of reasonably high confidence.

Biocyc NCBI Biosystems ==> Several gene sets from the "Biocyc" component of NCBI Biosystems: Geer LY, Marchler-Bauer A, Geer RC, Han L, He J, He S, Liu C, Shi W, Bryant SH (2010) The NCBI BioSystems database. Nucleic Acids Res. 38(Database issue):D492-6.

Kegg NCBI Biosystems ==> Several gene sets from the "Kegg" component of NCBI Biosystems: Geer LY et al 2010 (full citation above).

Palazzolo and Wang ==> These gene sets were compiled from a variety of sources by Mike Palazzolo and Jim Wang at CHDI.

Pathway Interaction Database NCBI Biosystems ==> Several gene sets from the "Pathway Interaction Database" component of NCBI Biosystems: Geer LY et al 2010 (full citation above).

PMID 17500595 Kaltenbach 2007 ==> Several gene sets from: Kaltenbach LS, Romero E, Becklin RR, Chettier R, Bell R, Phansalkar A, et al. (2007) Huntingtin interacting proteins are genetic modifiers of neurodegeneration. PLoS Genet. 3(5):e82

PMID 22348130 Schaefer 2012 ==> Several gene sets from: Schaefer MH, Fontaine JF, Vinayagam A, Porras P, Wanker EE, Andrade-Navarro MA (2012) HIPPIE: Integrating protein interaction networks with experiment based quality scores. PLoS One. 7(2):e31826

PMID 22556411 Culver 2012 ==> Several gene sets from: Culver BP, Savas JN, Park SK, Choi JH, Zheng S, Zeitlin SO, Yates JR 3rd, Tanese N. (2012) Proteomic analysis of wild-type and mutant huntingtin-associated proteins in mouse brains identifies unique interactions and involvement in protein synthesis. J Biol Chem. 287(26):21599-614

PMID 22578497 Cajigas 2012 ==> Several gene sets from: Cajigas IJ, Tushev G, Will TJ, tom Dieck S, Fuerst N, Schuman EM. (2012) The local transcriptome in the synaptic neuropil revealed by deep sequencing and high-resolution imaging. Neuron. 74(3):453-66

Reactome NCBI Biosystems ==> Several gene sets from the "Reactome" component of NCBI Biosystems: Geer LY et al 2010 (full citation above).

Wiki Pathways NCBI Biosystems ==> Several gene sets from the "Wiki Pathways" component of NCBI Biosystems: Geer LY et al 2010 (full citation above).

Yang ==> These gene sets were compiled from a variety of sources by Mike Palazzolo and Jim Wang at CHDI.

Examples

```
# Example: first, read in some gene names and split them into categories
data(BrainLists);
listGenes = unique(as.character(BrainLists[,1]))
set.seed(100)
geneR = sort(sample(listGenes, 2000))
categories = sort(rep(standardColors(10),200))
categories[sample(1:2000,200)] = "grey"
file1 = tempfile();
file2 = tempfile();
write(c("TESTLIST1",geneR[300:400], sep="\n"), file1)
write(c("TESTLIST2",geneR[800:1000],sep="\n"), file2)
# Now run the function!
testResults = userListEnrichment(
   geneR, labelR=categories,
   fnIn=c(file1, file2),
   catNmIn=c("TEST1","TEST2"),
   nameOut = NULL, useBrainLists=TRUE, omitCategories ="grey")
# To see a list of all significant enrichments type:
testResults$sigOverlaps
# To see all of the overlapping genes between two categories
#(whether or not the p-value is significant), type
#restResults$ovGenes$'<labelR> -- <comparisonCategory>'. For example:
testResults$ovGenes$"black -- TESTLIST1__TEST1"
```

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```
testResults$ovGenes$"red -- salmon_M12_Ribosome__HumanMeta"

# More detailed overlap information is in the pValue output. For example:
head(testResults$pValue)

# Clean up the temporary files
unlink(file1);
unlink(file2)
```

vectorizeMatrix

Turn a matrix into a vector of non-redundant components

Description

A convenient function to turn a matrix into a vector of non-redundant components. If the matrix is non-symmetric, returns a vector containing all entries of the matrix. If the matrix is symmetric, only returns the upper triangle and optionally the diagonal.

Usage

```
vectorizeMatrix(M, diag = FALSE)
```

Arguments

M the matrix or data frame to be vectorized.

diag logical: should the diagonal be included in the output?

Value

A vector containing the non-redundant entries of the input matrix.

Author(s)

Steve Horvath

vectorTOM

Topological overlap for a subset of the whole set of genes

Description

This function calculates topological overlap of a small set of vectors with respect to a whole data set.

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Usage

```
vectorTOM(
  datExpr,
  vect,
  subtract1 = FALSE,
  blockSize = 2000,
  corFnc = "cor", corOptions = "use = 'p'",
  networkType = "unsigned",
  power = 6,
  verbose = 1, indent = 0)
```

Arguments

datExpr a data frame containing the expression data of the whole set, with rows corre-

sponding to samples and columns to genes.

vect a single vector or a matrix-like object containing vectors whose topological over-

lap is to be calculated.

subtract1 logical: should calculation be corrected for self-correlation? Set this to TRUE if

vect contains a subset of datExpr.

blockSize maximum block size for correlation calculations. Only important if vect con-

tains a large number of columns.

corFnc character string giving the correlation function to be used for the adjacency cal-

culation. Recommended choices are "cor" and "bicor", but other functions

can be used as well.

corOptions character string giving further options to be passed to the correlation function.

networkType character string giving network type. Allowed values are (unique abbreviations

of) "unsigned", "signed", "signed hybrid". See adjacency.

power soft-thresholding power for network construction.

verbose integer level of verbosity. Zero means silent, higher values make the output

progressively more and more verbose.

indent indentation for diagnostic messages. Zero means no indentation, each unit adds

two spaces.

Details

Topological overlap can be viewed as the normalized count of shared neighbors encoded in an adjacency matrix. In this case, the adjacency matrix is calculated between the columns of vect and datExpr and the topological overlap of vectors in vect measures the number of shared neighbors in datExpr that vectors of vect share.

Value

A matrix of dimensions n*n, where n is the number of columns in vect.

Author(s)

Peter Langfelder

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References

Bin Zhang and Steve Horvath (2005) "A General Framework for Weighted Gene Co-Expression Network Analysis", Statistical Applications in Genetics and Molecular Biology: Vol. 4: No. 1, Article 17

See Also

TOMsimilarity for standard calculation of topological overlap.

verboseBarplot	Barplot with error bars, annotated by Kruskal-Wallis or ANOVA p-value
----------------	---

Description

Produce a barplot with error bars, annotated by Kruskal-Wallis or ANOVA p-value.

Usage

Arguments

X	numerical or binary vector of data whose group means are to be plotted
g	a factor or a an object coercible to a factor giving the groups whose means are to be calculated.
main	main title for the plot.
xlab	label for the x-axis.
ylab	label for the y-axis.
cex	character expansion factor for plot annotations.
cex.axis	character expansion factor for axis annotations.
cex.lab	character expansion factor for axis labels.

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cex.main character expansion factor for the main title.

color a vector giving the colors of the bars in the barplot.

numberStandardErrors

size of the error bars in terms of standard errors. See details.

KruskalTest logical: should Kruskal-Wallis test be performed? See details.

AnovaTest logical: should ANOVA be performed? See details.

two.sided logical: should the printed p-value be two-sided? See details.

addCellCounts logical: should counts be printed above each bar? horiz logical: should the bars be drawn horizontally?

ylim optional specification of the limits for the y axis. If not given, they will be

determined automatically.

... other parameters to function barplot.

addScatterplot logical: should a scatterplot of the data be overlaid?

pt.cex character expansion factor for the points.

pch shape code for the points.

pt.col color for the points.

pt.bg background color for the points.

randomSeed integer random seed to make plots reproducible.

jitter amount of random jitter to add to the position of the points along the x axis.

pointLabels Optional text labels for the points displayed using the scatterplot. If given,

should be a character vector of the same length as x. See labelPoints.

label.cex Character expansion (size) factor for pointLabels.label.offs Offset for pointLabels, as a fraction of the plot width.

adjustYLim logical: should the limits of the y axis be set so as to accommodate the indi-

vidual points? The adjustment is only carried out if input ylim is NULL and addScatterplot is TRUE. In particular, if the user supplies ylim, it is not touched.

Details

This function creates a barplot of a numeric variable (input x) across the levels of a grouping variable (input g). The height of the bars equals the mean value of x across the observations with a given level of g. By default, the barplot also shows plus/minus one standard error. If you want only plus one standard error (not minus) choose two.sided=TRUE. But the number of standard errors can be determined with the input numberStandardErrors. For example, if you want a 95% confidence interval around the mean, choose numberStandardErrors=2. If you don't want any standard errors set numberStandardErrors=-1. The function also outputs the p-value of a Kruskal Wallis test (Fisher test for binary input data), which is a non-parametric multi group comparison test. Alternatively, one can use Analysis of Variance (Anova) to compute a p-value by setting AnovaTest=TRUE. Anova is a generalization of the Student t-test to multiple groups. In case of two groups, the Anova p-value equals the Student t-test p-value. Anova should only be used if x follows a normal distribution. Anova also assumes homoscedasticity (equal variances). The Kruskal Wallis test is often advantageous since it makes no distributional assumptions. Since the Kruskal Wallis test is based on the ranks of x, it is more robust with regard to outliers. All p-values are two-sided.

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Value

None.

Author(s)

Steve Horvath, with contributions from Zhijin (Jean) Wu and Peter Langfelder

See Also

barplot

Examples

verboseBoxplot

Boxplot annotated by a Kruskal-Wallis p-value

Description

Plot a boxplot annotated by the Kruskal-Wallis p-value. Uses the function boxplot for the actual drawing.

Usage

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Arguments

a factor or a an object coercible to a factor giving the groups that will go into each box. main main title for the plot. xlab label for the x-axis. ylab label for the y-axis. cex character expansion factor for plot annotations. cex.axis character expansion factor for axis annotations. cex.lab character expansion factor for axis labels. cex.main character expansion factor for the main title. notch logical: should the notches be drawn? See boxplot and boxplot.stats for details. varwidth logical: if TRUE, the boxes are drawn with widths proportional to the square-roots of the number of observations in the groups. other arguments to the function boxplot. Of note is the argument las that specifies label orientation. Value las=1 will result in horizontal labels (the default), while las=2 will result in vertical labels, useful when the labels are long. addScatterplot logical: should a scatterplot of the data be overlaid? pt.cex character expansion factor for the points.
xlab label for the x-axis. ylab label for the y-axis. cex character expansion factor for plot annotations. cex.axis character expansion factor for axis annotations. cex.lab character expansion factor for axis labels. cex.main character expansion factor for the main title. notch logical: should the notches be drawn? See boxplot and boxplot.stats for details. varwidth logical: if TRUE, the boxes are drawn with widths proportional to the square-roots of the number of observations in the groups. other arguments to the function boxplot. Of note is the argument las that specifies label orientation. Value las=1 will result in horizontal labels (the default), while las=2 will result in vertical labels, useful when the labels are long. addScatterplot logical: should a scatterplot of the data be overlaid?
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ifies label orientation. Value las=1 will result in horizontal labels (the default), while las=2 will result in vertical labels, useful when the labels are long. addScatterplot logical: should a scatterplot of the data be overlaid?
•
pt.cex character expansion factor for the points.
pch shape code for the points.
pt.col color for the points.
pt.bg background color for the points.
randomSeed integer random seed to make plots reproducible.
jitter amount of random jitter to add to the position of the points along the x axis.

Value

Returns the value returned by the function boxplot.

Author(s)

Steve Horvath, with contributions from Zhijin (Jean) Wu and Peter Langfelder

See Also

boxplot

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verboseIplot So	catterplot with density
-----------------	-------------------------

Description

Produce a scatterplot that shows density with color and is annotated by the correlation, MSE, and regression line.

Usage

Arguments

X	numerical vector to be plotted along the x axis.
у	numerical vector to be plotted along the y axis.
xlim	define the range in x axis
ylim	define the range in y axis
nBinsX	number of bins along the x axis
nBinsY	number of bins along the y axis
ztransf	Function to transform the number of counts per pixel, which will be mapped by the function in colramp to well defined colors. The user has to make sure that the transformed density lies in the range [0,zmax], where zmax is any positive number (>=2).
gamma	color correction power
sample	either a number of points to be sampled or a vector of indices input x and y for points to be plotted. Useful when the input vectors are large and plotting all points is not practical.
corFnc	character string giving the correlation function to annotate the plot.
corOptions	character string giving further options to the correlation function.
main	main title for the plot.
xlab	label for the x-axis.
ylab	label for the y-axis.
cex	character expansion factor for plot annotations.

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character expansion factor for axis annotations. cex.axis cex.lab character expansion factor for axis labels. cex.main character expansion factor for the main title. abline logical: should the linear regression fit line be plotted? abline.color color specification for the fit line. abline.lty line type for the fit line. character string to be used as the label for the correlation value printed in the corLabel logical: should the MSE be added to the main title? showMSE

Details

Irrespective of the specified correlation function, the MSE is always calculated based on the residuals of a linear model.

Value

If sample above is given, the indices of the plotted points are returned invisibly.

other arguments to the function plot.

Note

This funtion is based on verboseScatterplot (Steve Horvath and Peter Langfelder), iplot (Andreas Ruckstuhl, Rene Locher) and greenWhiteRed(Peter Langfelder)

Author(s)

Chaochao Cai, Steve Horvath

See Also

image for more parameters

verboseScatterplot	Scatterplot annotated by regression line and p-value

Description

Produce a scatterplot annotated by the correlation, p-value, and regression line.

428 verboseScatterplot

Usage

Arguments

x numerical vector to be plotted along the x axis.

y numerical vector to be plotted along the y axis.

sample determines whether x and y should be sampled for plotting, useful to keep the

plot manageable when x and y are large vectors. The default NULL value implies no sampling. A single numeric value will be interpreted as the number of points to sample randomly. If a vector is given, it will be interpreted as the indices of the entries in x and y that should be plotted. In either case, the correlation and p

value will be determined from the full vectors x and y.

corFnc character string giving the correlation function to annotate the plot.

corOptions character string giving further options to the correlation function.

main main title for the plot.
xlab label for the x-axis.
ylab label for the y-axis.

cex character expansion factor for plot annotations, recycled as necessary.

cex.axis character expansion factor for axis annotations.

cex.lab character expansion factor for axis labels.
cex.main character expansion factor for the main title.

abline logical: should the linear regression fit line be plotted?

abline.color color specification for the fit line.

abline.lty line type for the fit line.

corLabel character string to be used as the label for the correlation value printed in the

main title.

displayAsZero Correlations whose absolute value is smaller than this number will be displayed

as zero. This can result in a more intuitive display (for example, cor=0 instead

of cor=2.6e-17).

col color of the plotted symbols. Recycled as necessary.

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bg	fill color of the plotted symbols (used for certain symbols). Recycled as necessary.
pch	Integer code for plotted symbols (see link{plot.default}). Recycled as necessary.
lmFnc	linear model fit function. Used to calculate the linear model fit line if 'abline' is TRUE. For example, robust linear models are implemented in the function rlm.
plotPriority	Optional numeric vector of same length as x. Points with higher plot priority will be plotted later, making them more visible if points overlap.
showPValue	Logical: should the p-value corresponding to the correlation be added to the title?
	other arguments to the function plot.

Details

Irrespective of the specified correlation function, the p-value is always calculated for pearson correlation.

Value

If sample above is given, the indices of the plotted points are returned invisibly.

Author(s)

Steve Horvath and Peter Langfelder

See Also

```
plot.default for standard scatterplots
```

```
votingLinearPredictor Voting linear predictor
```

Description

Predictor based on univariate regression on all or selected given features that pools all predictions using weights derived from the univariate linear models.

Usage

```
votingLinearPredictor(
    x, y, xtest = NULL,
    classify = FALSE,
    CVfold = 0,
    randomSeed = 12345,
    assocFnc = "cor", assocOptions = "use = 'p'",
    featureWeightPowers = NULL, priorWeights = NULL,
```

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```
weighByPrediction = 0,
nFeatures.hi = NULL, nFeatures.lo = NULL,
dropUnusedDimensions = TRUE,
verbose = 2, indent = 0)
```

Arguments

xtest

classify

CVfold

randomSeed

assocFnc

assocOptions

priorWeights

X	Training features (predictive variables). Each column corresponds to a feature
	and each row to an observation.

y The response variable. Can be a single vector or a matrix with arbitrary many columns. Number of rows (observations) must equal to the number of rows (observations) in x.

Optional test set data. A matrix of the same number of columns (i.e., features) as x. If test set data are not given, only the prediction on training data will be returned.

Should the response be treated as a categorical variable? Classification really only works with two classes. (The function will run for multiclass problems as well, but the results will be sub-optimal.)

Optional specification of cross-validation fold. If 0 (the default), no cross-validation is performed.

Random seed, used for observation selection for cross-validation. If NULL, the random generator is not reset.

Function to measure association. Usually a measure of correlation, for example Pearson correlation or bicor.

Character string specifying the options to be passed to the association function.

featureWeightPowers

Powers to which to raise the result of assocFnc to obtain weights. Can be a single number or a vector of arbitrary length; the returned value will contain one prediction per power.

Prior weights for the features. If given, must be either (1) a vector of the same length as the number of features (columns in x); (2) a matrix of dimensions length(featureWeightPowers)x(number of features); or (3) array of dimensions (number of response variables)xlength(featureWeightPowers)x(number of features).

weighByPrediction

(Optional) power to downweigh features that are not well predicted between training and test sets. See details.

nFeatures.hi Optional restriction of the number of features to use. If given, this many features with the highest association and lowest association (if nFeatures.lo is not given) will be used for prediction.

nFeatures.10 Optional restriction of the number of lowest (i.e., most negatively) associated features to use. Only used if nFeatures.hi is also non-NULL.

dropUnusedDimensions

Logical: should unused dimensions be dropped from the result?

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verbose Integer controling how verbose the diagnostic messages should be. Zero means

silent.

indent Indentation for the diagnostic messages. Zero means no indentation, each unit

adds two spaces.

Details

The predictor calculates the association of each (selected) feature with the response and uses the association to calculate the weight of the feature as sign(association) * (association)^featureWeightPower. Optionally, this weight is multiplied by priorWeights. Further, a feature prediction weight can be used to downweigh features that are not well predicted by other features (see below).

For classification, the (continuous) result of the above calculation is turned into ordinal values essentially by rounding.

If features exhibit non-trivial correlations among themselves (such as, for example, in gene expression data), one can attempt to down-weigh features that do not exhibit the same correlation in the test set. This is done by using essentially the same predictor to predict _features_ from all other features in the test data (using the training data to train the feature predictor). Because test features are known, the prediction accuracy can be evaluated. If a feature is predicted badly (meaning the error in the test set is much larger than the error in the cross-validation prediction in training data), it may mean that its quality in the training or test data is low (for example, due to excessive noise or outliers). Such features can be downweighed using the argument weighByPrediction. The extra factor is min(1, (root mean square prediction error in test set)/(root mean square cross-validation prediction error in the training data)^weighByPrediction), that is it is never bigger than 1.

Value

A list with the following components:

predicted The back-substitution prediction on the training data. Normally an array of di-

mensions (number of observations) x (number of response variables) x length(featureWeightPowers),

but unused are dropped unless dropUnusedDimensions = FALSE.

weightBase Absolute value of the associations of each feature with each response.

variableImportance

The weight of each feature in the prediction (including the sign).

predictedTest If input xtest is non-NULL, the predicted test response, in format analogous to

predicted above.

CVpredicted If input CVfold is non-zero, cross-validation prediction on the training data.

Note

It makes little practical sense to supply neither xtest nor CVfold since the prediction accuracy on training data will be highly biased.

Author(s)

Peter Langfelder

See Also

bicor for robust correlation that can be used as an association measure

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