Package 'Patterns'

January 20, 2025

Type Package

Title Deciphering Biological Networks with Patterned Heterogeneous Measurements

Version 1.5

Date 2024-05-03

Depends R (>= 3.5.0)

Imports abind, cluster, e1071, gplots, graphics, grDevices, igraph, jetset, lars, lattice, limma, methods, Mfuzz, movMF, nnls, plotrix, repmis, SelectBoost, tnet, VGAM, WGCNA

Suggests animation, Biobase, biomaRt, c060, CascadeData, elasticnet, glmnet, knitr, pixmap, R.rsp, rmarkdown, spls

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Description A modeling tool dedicated to biological network modeling (Bertrand and others 2020, <doi:10.1093/bioinformatics/btaa855>). It allows for single or joint modeling of, for instance, genes and proteins. It starts with the selection of the actors that will be the used in the reverse engineering upcoming step. An actor can be included in that selection based on its differential measurement (for instance gene expression or protein abundance) or on its time course profile. Wrappers for actors clustering functions and cluster analysis are provided. It also allows reverse engineering of biological networks taking into account the observed time course patterns of the actors. Many inference functions are provided and dedicated to get specific features for the inferred network such as sparsity, robust links, high confidence links or stable through resampling links. Some simulation and prediction tools are also available for cascade networks (Jung and others 2014, <doi:10.1093/bioinformatics/btt705>). Example of use with microarray or RNA-Seq data are provided.

Encoding UTF-8

Collate Patterns-package.R global.R datasets.R omics_array.R omics_network.R omics_array-omics_network.R omics_predict.R

Classification/MSC 62J05, 62J07, 62J99, 92C42

VignetteBuilder knitr

RoxygenNote 7.3.1

URL https://fbertran.github.io/Patterns/,
https://github.com/fbertran/Patterns/

BugReports https://github.com/fbertran/Patterns/issues/

NeedsCompilation no

Repository CRAN

Date/Publication 2024-05-06 13:40:02 UTC

Contents

`analyze_network,omics_network-method`
Analysing the network

Description

Calculates some indicators for each node in the network.

Usage

```
## S4 method for signature 'omics_network'
analyze_network(Omega, nv, label_v = NULL)
```

Arguments

`Omega`	a omics_network object
`nv`	the level of cutoff at which the analysis should be done
`label_v`	(optionnal) the name of the genes

Value

A matrix containing, for each node, its betweenness,its degree, its output, its closeness.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(network)
analyze_network(network,nv=0)
```

`as.omics_array` *Coerce a matrix into a omics_array object.*

Description

Coerce a matrix into a omics_array object.

Usage

```
as.omics_array(
  M,
  time,
  subject,
  name_probe = NULL,
  gene_ID = NULL,
  group = 0,
  start_time = 0
)
```

Arguments

`M`	A matrix. Contains the omicsarray measurements. Should be of size N * K, with N the number of genes and K=T*P with T the number of time points, and P the number of subjects. This matrix should be created using cbind(M1,M2,...) with M1 a N*T matrix with the measurements for patient 1, M2 a N*T matrix with the measurements for patient 2.
`time`	A vector. The time points measurements
`subject`	The number of subjects.
`name_probe`	Vector with the row names of the omics array.
`gene_ID`	Vector with the actors' IDs of the row names of the omics array.
`group`	Vector with the actors' groups of the row names of the omics array.
`start_time`	Vector with the actors' starting time (i.e. the time it is thought to begin to have an effect on another actor in the network).

Value

A omics_array object.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
if(require(CascadeData)){
data(micro_US, package="CascadeData")
micro_US<-as.omics_array(micro_US[1:100,],time=c(60,90,210,390),subject=6)
plot(micro_US)
}
```

CascadeFinit *Create initial F matrices for cascade networks inference.*

Description

This is an helper function to create initial values F matrices for cascade networks.

Usage

```
CascadeFinit(sqF, ngrp, low.trig = TRUE)
```

Arguments

sqF	Size of an F cell
ngrp	Number of groups
low.trig	Fill the lower trigonal matrices with ones

Value

An array of sizes c(sqF, sqF, ngrp).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
CascadeFinit(3,2)
CascadeFinit(4,3)
plotF(CascadeFinit(4,3),choice = "F")
CascadeFinit(3,2,low.trig=FALSE)
CascadeFinit(4,3,low.trig=FALSE)
plotF(CascadeFinit(4,3,low.trig=FALSE),choice = "F")
```

CascadeFshape — *Create F matrices shaped for cascade networks inference.*

Description

This is an helper function to create F matrices with special shape used for cascade networks.

Usage

```
CascadeFshape(sqF, ngrp)
```

Arguments

sqF	Size of an F cell
ngrp	Number of groups

Value

An array of sizes c(sqF, sqF, ngrp).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
CascadeFshape(3,2)
plotF(CascadeFshape(3,2),choice = "Fshape")
CascadeFshape(4,3)
plotF(CascadeFshape(4,3),choice = "Fshape")
```

CLL — *Expression data from healthy and malignant (chronic lymphocytic leukemia, CLL) human B-lymphocytes after B-cell receptor stimulation (GSE 39411 dataset)*

Description

B-cells were negatively selected from healthy donors and previously untreated CLL patients. BCR stimulated and unstimulated control B-cells were treated at four time points after stimulation for total RNA extraction and hybridization on Affymetrix microarrays.

Format

The format is: chr "CLL"

Details

The dataset provided with package is the first five lines of the full dataset. The full dataset can be downloaded from the github repository of the package (https://raw.githubusercontent.com/fbertran/Patterns/master/add_data/

Three different cell populations (6 healthy B-lymphocytes, 6 leukemic CLL B-lymphocyte of indolent form and 5 leukemic CLL B-lymphocyte of aggressive form) were stimulated in vitro with an anti-IgM antibody, activating the B-cell receptor (BCR). We analyzed the gene expression at 4 time points (60, 90, 210 and 390 minutes). Each gene expression measurement is performed both in stimulated cells and in control unstimulated cells. For one aggressive CLL case, we silenced expression of DUSP1 by transfecting DUSP1-specific RNAi and, as a control, transfected cells with a non-targeting RNAi. We then stimulated the BCR of these cells and analyzed the gene expression at the same time points in stimulated cells and in control unstimulated cells.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Source

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE39411

References

Vallat, L., Kemper, C. A., Jung, N., Maumy-Bertrand, M., Bertrand, F., Meyer, N., ... Bahram, S. (2013). Reverse-engineering the genetic circuitry of a cancer cell with predicted intervention in chronic lymphocytic leukemia. Proceedings of the National Academy of Sciences of the United States of America, 110(2), 459–464.

Examples

```
data(CLL)
str(CLL)


CLLfile <- "https://github.com/fbertran/Patterns/raw/master/add_data/CLL.RData"
repmis::source_data(CLLfile)
str(CLL)
```

`clustExploration,omics_array-method`

A function to explore a dataset and cluster its rows.

Description

Based on soft clustering performed by the Mfuzz package.

Usage

```
## S4 method for signature 'omics_array'
clustExploration(omicsarray, new.window = FALSE)
```

Arguments

omicsarray	A omicsarray to cluster
new.window	Boolean. New X11 window for plots. Defaults to FALSE.

Value

A data.frame of nrows(omicsarray) observations of 3 variables (name, cluster, maj.vote.index).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
library(Patterns)
if(require(CascadeData)){
data(micro_S, package="CascadeData")
D<-Patterns::as.omics_array(micro_S[1:100,],1:4,6)
a<-clustExploration(D)
a
}
```

---

clustInference,omics_array,numeric-method

A function to explore a dataset and cluster its rows.

Description

Based on soft clustering performed by the Mfuzz package.

Usage

```
## S4 method for signature 'omics_array,numeric'
clustInference(omicsarray, vote.index, new.window = FALSE)
```

Arguments

omicsarray	A omicsarray to cluster
vote.index	Option for cluster attribution
new.window	Boolean. New X11 window for plots. Defaults to FALSE.

Value

A list of two elements:

res.matrix	A data.frame of nrows(omicsarray) observations of 3 variables (name, cluster, maj.vote.index).
prop.matrix	Additionnal info.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
library(Patterns)
if(require(CascadeData)){
data(micro_S, package="CascadeData")
D<-Patterns::as.omics_array(micro_S[1:20,],1:4,6)
b<-Patterns::clustInference(D,0.5)
b
}
```

---

compare-methods *Some basic criteria of comparison between actual and inferred network.*

Description

Allows comparison between actual and inferred network.

Usage

```
## S4 method for signature 'omics_network,omics_network,numeric'
compare(Net, Net_inf, nv = 1)
```

Arguments

Net	A omics_network object containing the actual network.
Net_inf	A omics_network object containing the inferred network.
nv	A number that indicates at which level of cutoff the comparison should be done.

Value

A vector containing : sensitivity, predictive positive value, the usual F-score (2*ppv*sens/(sppvpe+sens)),
the 1/2 ponderated Fscore ((1+0.5^2)*ppv*sens/(ppv/4+sens)) and the 2 ponderated Fscore ((1+2^2)*ppv*sens/(ppv*4+sens)

Methods

list("signature(Net = \"omics_network\", Net_inf = \"omics_network\", nv = \"numeric\")") Net A omics_network object containing the actual network.

Net_inf A omics_network object containing the inferred network.

nv A number that indicates at which level of cutoff the comparison should be done.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Net)
data(Net_inf_PL)

#Comparing true and inferred networks
Crit_values=NULL

#Here are the cutoff level tested
test.seq<-seq(0,max(abs(Net_inf_PL@omics_network*0.9)),length.out=200)
for(u in test.seq){
Crit_values<-rbind(Crit_values,Patterns::compare(Net,Net_inf_PL,u))
}
matplot(test.seq,Crit_values,type="l",ylab="Criterion value",xlab="Cutoff level",lwd=2)
legend(x="topleft", legend=colnames(Crit_values), lty=1:5,col=1:5,ncol=2,cex=.9)
```

---

cutoff,omics_network-method

Choose the best cutoff

Description

Allows estimating the best cutoff. For a sequence of cutoff, the p value corresponding to each cutoff value of the sequence. Mainly recommended for single time cascade networks. To achieve more sparsity in other settings, please use a fiiting function based on the stability selection or selectboost algorithms.

Usage

```
## S4 method for signature 'omics_network'
cutoff(Omega, sequence = NULL, x_min = 0)
```

Arguments

Omega	a omics_network object
sequence	a vector corresponding to the sequence of cutoffs that will be tested.
x_min	an integer ; only values over x_min are further retained for performing the test.

Value

A list containing two objects :

`p.value`	the p values corresponding to the sequence of cutoff
`p.value.inter`	the smoothed p value vector, using the loess function

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(network)
cutoff(network)
#See vignette for more details
```

`dim` *Dimension of the data*

Description

Dimension of the data

Usage

```
## S4 method for signature 'omics_array'
dim(x)
```

Arguments

`x`	an object of class ‘omics_array‘.

Methods

list("signature(x = \"omics_array\")") Gives the dimension of the matrix of measurements.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

doc *Human transcription factors from HumanTFDB*

Description

Retrieve human transcription factors from HumanTFDB, extracted from AnimalTFDB 3.0: a comprehensive resource for annotation and prediction of animal transcription factors. Hui Hu, Ya-Ru Miao, Long-Hao Jia, Qing-Yang Yu, Qiong Zhang and An-Yuan Guo. *Nucl. Acids Res*. (2018).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(doc)
head(doc)
summary(doc)
```

evolution,omics_network-method *See the evolution of the network with change of cutoff*

Description

See the evolution of the network with change of cutoff

Usage

```
## S4 method for signature 'omics_network'
evolution(
  net,
  list_nv,
  gr = NULL,
  color.vertex = NULL,
  color.edge = NULL,
  fix = TRUE,
  size = c(2000, 1000),
  label_v = 1:dim(net@omics_network)[1],
  legend.position = "topleft",
  frame.color = "black",
  label.hub = FALSE,
  outdir,
  type.ani = "html"
)
```

Arguments

net	a omics_network object
list_nv	a vector of cutoff at which the network should be shown
gr	a vector giving the group of each genee. Defaults to NULL
color.vertex	a vector giving the color of each nodee. Defaults to NULL
color.edge	a vector giving the color of each edge. Defaults to NULL
fix	logical, should the position of the node in the network be calculated once at the beginning ? Defaults to TRUE.
size	vector giving the size of the plot. Defaults to c(2000,1000)
label_v	vector giving the labels of each vertex. Defaults to 1:dim(net@omics_network)[1]
legend.position	string giving the position of the legend. Defaults to "topleft"
frame.color	string giving the color of the frame of the plot. Defaults to "black"
label.hub	label hubs. Defaults to FALSE
outdir	Directory to save the animation. No default value since it must be specified by the user.
type.ani	Type of animation. Defaults to "html"
legend	string giving the position of the legend. Defaults to "topleft"

Details

Several types of outputs are available using the type.ani option.

- html
- latex (requires latex)
- swf (requires swftools)
- video (requires ffmpeg)
- gif
- manual_gif

Value

A HTML page with the evolution of the network.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(network)
sequence<-seq(0,0.2,length.out=20)

#Change the destdir to have the animation created where you want.
destdir = tempdir()

#Example of use of the evolution method with an html output.
evolution(network,sequence,type.ani = "html", outdir=destdir)


## Not run:
#Example of use of the evolution method with an animated gif output.
evolution(network,sequence,type.ani = "gif", outdir=destdir)

## End(Not run)
```

---

geneNeighborhood,omics_network-method

Find the neighborhood of a set of nodes.

Description

Find the neighborhood of a set of nodes.

Usage

```
## S4 method for signature 'omics_network'
geneNeighborhood(
  net,
  targets,
  nv = 0,
  order = length(net@time_pt) - 1,
  label_v = NULL,
  ini = NULL,
  frame.color = "white",
  label.hub = FALSE,
  graph = TRUE,
  names = F
)
```

Arguments

net	a omics_network object
targets	a vector containing the set of nodes

nv	the level of cutoff. Defaut to 0.
order	of the neighborhood. Defaut to 'length(net@time_pt)-1'.
label_v	vector defining the vertex labels.
ini	using the "position" function, you can fix the position of the nodes.
frame.color	color of the frames.
label.hub	logical ; if TRUE only the hubs are labeled.
graph	plot graph of the network. Defaults to 'TRUE'.
names	return names of the neighbors. Defaults to 'FALSE'.

Value

The neighborhood of the targeted genes.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Selection)
data(infos)
#Find probesets for EGR1
pbst_EGR1 = infos[infos$hgnc_symbol=="EGR1", "affy_hg_u133_plus_2"]

gene_IDs = infos[match(Selection@name, infos$affy_hg_u133_plus_), "hgnc_symbol"]

data(network)
#A nv value can chosen using the cutoff function
nv=.11
EGR1<-which(is.element(Selection@name,pbst_EGR1))
P<-position(network,nv=nv)

geneNeighborhood(network,targets=EGR1,nv=nv,ini=P,
label_v=gene_IDs)
```

---

geneSelection *Methods for selecting genes*

Description

Selection of differentially expressed genes.

Usage

```
## S4 method for signature 'omics_array,omics_array,numeric'
geneSelection(
  x,
  y,
  tot.number,
  data_log = TRUE,
  wanted.patterns = NULL,
  forbidden.patterns = NULL,
  peak = NULL,
  alpha = 0.05,
  Design = NULL,
  lfc = 0
)

## S4 method for signature 'list,list,numeric'
geneSelection(
  x,
  y,
  tot.number,
  data_log = TRUE,
  alpha = 0.05,
  cont = FALSE,
  lfc = 0,
  f.asso = NULL,
  return.diff = FALSE
)

## S4 method for signature 'omics_array,numeric'
genePeakSelection(
  x,
  peak,
  y = NULL,
  data_log = TRUE,
  durPeak = c(1, 1),
  abs_val = TRUE,
  alpha_diff = 0.05
)
```

Arguments

x	either a omics_array object or a list of omics_array objects. In the first case, the omics_array object represents the stimulated measurements. In the second case, the control unstimulated data (if present) should be the first element of the list.
y	either a omics_array object or a list of strings. In the first case, the omics_array object represents the stimulated measurements. In the second case, the list is the way to specify the contrast:

First element: condition, condition&time or pattern. The condition specification is used when the overall is to compare two conditions. The condition&time specification is used when comparing two conditions at two precise time points. The pattern specification allows to decide which time point should be differentially expressed.

Second element: a vector of length 2. The two conditions which should be compared. If a condition is used as control, it should be the first element of the vector. However, if this control is not measured throught time, the option cont=TRUE should be used.

Third element: depends on the first element. It is no needed if condition has been specified. If condition&time has been specified, then this is a vector containing the time point at which the comparison should be done. If pattern has been specified, then this is a vector of 0 and 1 of length T, where T is the number of time points. The time points with desired differential expression are provided with 1.

`tot.number` an integer. The number of selected genes. If tot.number <0 all differentially genes are selected. If tot.number > 1, tot.number is the maximum of diffenrtially genes that will be selected. If 0<tot.number<1, tot.number represents the proportion of diffenrentially genes that are selected.

`data_log` logical (default to TRUE); should data be logged ?

`wanted.patterns`
a matrix with wanted patterns [only for geneSelection].

`forbidden.patterns`
a matrix with forbidden patterns [only for geneSelection].

`peak` interger. At which time points measurements should the genes be selected [optionnal for geneSelection].

`alpha` float; the risk level. Default to 'alpha=0.05'

`Design` the design matrix of the experiment. Defaults to 'NULL'.

`lfc` log fold change value used in limma's 'topTable'. Defaults to 0.

`cont` use contrasts. Defaults to 'FALSE'.

`f.asso` function used to assess the association between the genes. The default value 'NULL' implies the use of the usual 'mean' function.

`return.diff` [FALSE] if TRUE then the function returns the stimulated expression of the differentially expressed genes

`durPeak` vector of size 2 (default to c(1,1)) ; the first elements gives the length of the peak at the left, the second at the right. [only for genePeakSelection]

`abs_val` logical (default to TRUE) ; should genes be selected on the basis of their absolute value expression ? [only for genePeakSelection]

`alpha_diff` float; the risk level

Value

A omics_array object.

Author(s)

Frédéric Bertrand , Myriam Maumy-Bertrand.

Examples

```
 if(require(CascadeData)){
data(micro_US)
micro_US<-as.omics_array(micro_US,time=c(60,90,210,390),subject=6)
data(micro_S)
micro_S<-as.omics_array(micro_S,time=c(60,90,210,390),subject=6)

  #Basically, to find the 50 more significant expressed genes you will use:
  Selection_1<-geneSelection(x=micro_S,y=micro_US,
  tot.number=50,data_log=TRUE)
  summary(Selection_1)

  #If we want to select genes that are differentially
  #at time t60 or t90 :
  Selection_2<-geneSelection(x=micro_S,y=micro_US,tot.number=30,
  wanted.patterns=
  rbind(c(0,1,0,0),c(1,0,0,0),c(1,1,0,0)))
  summary(Selection_2)

 #To select genes that have a differential maximum of expression at a specific time point.

  Selection_3<-genePeakSelection(x=micro_S,y=micro_US,peak=1,
  abs_val=FALSE,alpha_diff=0.01)
  summary(Selection_3)
  }

if(require(CascadeData)){
data(micro_US)
micro_US<-as.omics_array(micro_US,time=c(60,90,210,390),subject=6)
data(micro_S)
micro_S<-as.omics_array(micro_S,time=c(60,90,210,390),subject=6)
#Genes with differential expression at t1
Selection1<-geneSelection(x=micro_S,y=micro_US,20,wanted.patterns= rbind(c(1,0,0,0)))
#Genes with differential expression at t2
Selection2<-geneSelection(x=micro_S,y=micro_US,20,wanted.patterns= rbind(c(0,1,0,0)))
#Genes with differential expression at t3
Selection3<-geneSelection(x=micro_S,y=micro_US,20,wanted.patterns= rbind(c(0,0,1,0)))
#Genes with differential expression at t4
Selection4<-geneSelection(x=micro_S,y=micro_US,20,wanted.patterns= rbind(c(0,0,0,1)))
#Genes with global differential expression
Selection5<-geneSelection(x=micro_S,y=micro_US,20)

#We then merge these selections:
Selection<-unionOmics(list(Selection1,Selection2,Selection3,Selection4,Selection5))
print(Selection)

#Prints the correlation graphics Figure 4:
```

```
summary(Selection,3)

##Uncomment this code to retrieve geneids.
#library(org.Hs.eg.db)
#
#ff<-function(x){substr(x, 1, nchar(x)-3)}
#ff<-Vectorize(ff)
#
##Here is the function to transform the probeset names to gene ID.
#
#library("hgu133plus2.db")
#
#probe_to_id<-function(n){
#x <- hgu133plus2SYMBOL
#mp<-mappedkeys(x)
#xx <- unlist(as.list(x[mp]))
#genes_all = xx[(n)]
#genes_all[is.na(genes_all)]<-"unknown"
#return(genes_all)
#}
#Selection@name<-probe_to_id(Selection@name)
  }
```

---

gene_expr_simulation,omics_network-method

Simulates omicsarray data based on a given network.

Description

Simulates omicsarray data based on a given network.

Usage

```
## S4 method for signature 'omics_network'
gene_expr_simulation(
  omics_network,
  time_label = 1:4,
  subject = 5,
  peak_level = 100,
  act_time_group = 1:4
)
```

Arguments

omics_network	A omics_network object.
time_label	a vector containing the time labels.

subject	the number of subjects
peak_level	the mean level of peaks.
act_time_group	[NULL] vector ; at which time the groups (defined by sort(unique(group))) are activated ?

Value

A omics_array object.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Net)
set.seed(1)

#We simulate gene expressions according to the network Net
Msim<-Patterns::gene_expr_simulation(
omics_network=Net,
time_label=rep(1:4,each=25),
subject=5,
peak_level=200)
head(Msim)
```

---

head,omics_array-method

Overview of a omics_array object

Description

Overview of a omics_array object.

Usage

```
## S4 method for signature 'omics_array'
head(x, ...)
```

Arguments

x	an object of class ‘omics_array‘.
...	additional parameters

Methods

list("signature(x = \"ANY\")") Gives an overview.

list("signature(x = \"omics_array\")") Gives an overview.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
 if(require(CascadeData)){
data(micro_US)
micro_US<-as.omics_array(micro_US,time=c(60,90,210,390),subject=6)
head(micro_US)
}
```

IndicFinit — *Create initial F matrices using specific intergroup actions for network inference.*

Description

This is an helper function to create initial values F matrices for networks.

Usage

```
IndicFinit(sqF, ngrp, Indic, low.trig = TRUE)
```

Arguments

sqF	Size of an F cell
ngrp	Number of groups
Indic	Matrix to specify where there is an interaction from one group to another
low.trig	Fill the lower trigonal matrices with ones

Value

An array of size (sqF, sqF, ngrp).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
IndicFinit(3, 2, matrix(1,2,2)-diag(2))
```

`IndicFshape` *Create F matrices using specific intergroup actions for network inference.*

Description

This is an helper function to create values F matrices using specific intergroup actions for network inference.

Usage

```
IndicFshape(sqF, ngrp, Indic)
```

Arguments

`sqF`	Size of an F cell
`ngrp`	Number of groups
`Indic`	Matrix to specify where there is an interaction from one group to another

Value

An array of size (sqF, sqF, ngrp).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
IndicFshape(3, 2, matrix(1,2,2)-diag(2))
```

`inference` *Reverse-engineer the network*

Description

Reverse-engineer the network.

Usage

```
## S4 method for signature 'omics_array'
inference(
  M,
  tour.max = 30,
  g = function(x) {
     1/x
 },
  conv = 0.001,
  cv.subjects = TRUE,
  nb.folds = NULL,
  eps = 10^-5,
  type.inf = "iterative",
  Fshape = NULL,
  Finit = NULL,
  Omega = NULL,
  fitfun = "LASSO",
  use.Gram = TRUE,
  error.stabsel = 0.05,
  pi_thr.stabsel = 0.6,
  priors = NULL,
  mc.cores = getOption("mc.cores", 2L),
  intercept.stabpath = TRUE,
  steps.seq = 0.95,
  limselect = 0.95,
  use.parallel = TRUE,
  verbose = TRUE,
  show.error.messages = FALSE
)
```

Arguments

M	a omics_array object.
tour.max	[30] tour.max + 1 = maximal number of steps.
g	After each step, the new solution is choosen as (the old solution + g(x) * the new solution)/(1+g(x)) where x is the number of steps. Defaults to 'g=function(x) 1/x'
conv	[0.001] Convergence criterion.
cv.subjects	[TRUE] Subjectwise cross validation: should the cross validation be done by removing the subject one by one?
nb.folds	[NULL] Relevant only if no subjectwise cross validation (i.e. cv.subjects=FALSE). The number of folds in cross validation.
eps	[10^-5] Threshold for rounding coefficients to 0 (i.e. machine zero).
type.inf	["iterative"] "iterative" or "noniterative" : should the algorithm be computed iteratively or only for one step? For highly homogeneous clusters, the "noniterative" option is suffisant.

`Fshape` [NULL] Shape of the F matrix.

`Finit` [NULL] Init values of the F matrix.

`Omega` [NULL] Init values for the Omega matrix.

`fitfun` ["LASSO"] Function to infer the Omega matrix at each step.

`use.Gram` [TRUE] Optional parameter for the lasso in the 'lars' package.

`error.stabsel` [0.05] Optional parameter for the stability selection algorithm in the 'c060' package.

`pi_thr.stabsel` [0.6] Optional parameter for the stability selection algorithm in the 'c060' package.

`priors` [NULL] A priori weights for the links between the actors. 0 means that an actor is always included in the predictive model, 1 is a neutral weighting and +infinity that the actor is never used in the model. For a given predictive model, the weighting vector is normalized so that its sum is equal to the number of predictors in the model.

`mc.cores` [getOption("mc.cores", 2L)] Number of cores.

`intercept.stabpath` [TRUE] Use intercept in stability selection models?

`steps.seq` [.95] Optional parameter for the SelectBoost algorithm in the 'SelectBoost' package.

`limselect` [.95] Optional parameter for the SelectBoost algorithm in the 'SelectBoost' package.

`use.parallel` [TRUE] Use parallel computing?

`verbose` [TRUE] Info on the completion of the fitting process

`show.error.messages` [FALSE] Should the error messages of the Omega estimating function be returned?

Details

The fitting built-in fitting functions ('fitfun') provided with the 'Patterns' package are :

LASSO from the 'lars' package (default value)

LASSO2 from the 'glmnet' package

SPLS from the 'spls' package

ELASTICNET from the 'elasticnet' package

stability.c060 from the 'c060' package implementation of stability selection

stability.c060.weighted a new weighted version of the 'c060' package implementation of stability selection

robust lasso from the 'lars' package with light random Gaussian noise added to the explanatory variables

selectboost.weighted a new weighted version of the 'selectboost' package implementation of the selectboost algorithm to look for the more stable links against resampling that takes into account the correlated structure of the predictors. If no weights are provided, equal weigths are for all the variables (=non weighted case).

The weights are viewed as a penalty factors in the penalized regression model: it is a number that multiplies the lambda value in the minimization problem to allow differential shrinkage, [Friedman et al. 2010](https://web.stanford.edu/~hastie/Papers/glmnet.pdf), equation 1 page 3. If equal to 0, it implies no shrinkage, and that variable is always included in the model. Default is 1 for all variables. Infinity means that the variable is excluded from the model. Note that the weights are rescaled to sum to the number of variables.

Value

A omics_network object.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
#With simulated data, default shaped F matrix and default LASSO from the lars package
#as fitting function
data(M)
infM <- inference(M)
str(infM)
plot(infM, choice="F", nround=0)
plot(infM, choice="F", nround=1)

#With simulated data, cascade network shaped F matrix (1 group per time measurement case)
#and default LASSO from the lars package as fitting function
infMcasc <- inference(M, Finit=CascadeFinit(4,4), Fshape=CascadeFshape(4,4))
str(infMcasc)
plot(infMcasc, choice="F", nround=0)
plot(infMcasc, choice="F", nround=1)

#With selection of genes from GSE39411
data(Selection)
infSel <- inference(Selection, Finit=CascadeFinit(4,4), Fshape=CascadeFshape(4,4))
str(infSel)
str(infSel)
plot(infSel, choice="F", nround=0)
plot(infSel, choice="F", nround=1)
```

---

infos *Details on some probesets of the affy_hg_u133_plus_2 platform.*

Description

Dataset with information on the affy_hg_u133_plus_2 platform such as probeset name (affy_hg_u133_plus_2), ensembl_gene_id, entrezgene, hgnc_symbol, chromosome_name, start_position, end_position and band.

Format

The format is: chr "infos"

Details

Data.frame with 8859 rows and 8 variables.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(infos)
```

M *Simulated microarray.*

Description

Simulated M, microarray.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(M)
head(M)
str(M)
```

Net *Simulated network for examples.*

Description

Simulated network.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Net)
str(Net)
```

`network` *A example of an inferred network (4 groups case).*

Description

This dataset is a network example with 102 nodes, 4 times and 4 groups.

Format

The format is: chr "network"

Details

A network class object [package "Patterns"] with 6 slots.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(network)
str(network)
plot(network)
```

`network2gp` *A example of an inferred cascade network (2 groups case).*

Description

This dataset is a cascade network example with 53 nodes, 4 times and 2 groups.

Format

The format is: chr "network2gp"

Details

A network class object [package "Patterns"] with 6 slots.

Examples

```
data(network2gp)
str(network2gp)
plot(network2gp)
```

`networkCascade` *A example of an inferred cascade network (4 groups case).*

Description

This dataset is a cascade network example with 102 nodes, 4 times and 4 groups.

Format

The format is: chr "networkCascade"

Details

A network class object [package "Patterns"] with 6 slots.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(networkCascade)
str(networkCascade)
plot(networkCascade)
```

`network_random` *Generates a network.*

Description

Generates a network.

Usage

```
network_random(
  nb,
  time_label,
  exp,
  init,
  regul,
  min_expr,
  max_expr,
  casc.level
)
```

Arguments

nb	Integer. The number of genes.
time_label	Vector. The time points measurements.
exp	The exponential parameter, as in the barabasi.game function in igraph package.
init	The attractiveness of the vertices with no adjacent edges. See barabasi.game function.
regul	A vector mapping each gene with its number of regulators.
min_expr	Minimum of strength of a non-zero link
max_expr	Maximum of strength of a non-zero link
casc.level	...

Value

A omics_network object.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
set.seed(1)
Net<-network_random(
nb=100,
time_label=rep(1:4,each=25),
exp=1,
init=1,
regul=round(rexp(100,1))+1,
min_expr=0.1,
max_expr=2,
casc.level=0.4
)
plot(Net)
```

Net_inf_PL *Reverse-engineered network of the M and Net simulated data.*

Description

The reverse-engineered network with the 'Patterns' package using the fitfun="LASSO" default function and a cascade network setting.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Net_inf_PL)
str(Net_inf_PL)
```

omics_array-class *Class* "omics_array"

Description

The "omics_array" class

Objects from the Class

Objects can be created by calls of the form new("omics_array", ...).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
showClass("omics_array")
```

omics_network-class *Class* "omics_network"

Description

The "omics_network" class

Objects from the Class

Objects can be created by calls of the form new("omics_network", ...).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
showClass("omics_network")
```

omics_predict-class *Class* "omics_predict"

Description

The "omics_predict" class

Objects from the Class

Objects can be created by calls of the form new("omics_predict", ...).

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
showClass("omics_predict")
```

plot-methods *Plot*

Description

Considering the class of the argument which is passed to plot, the graphical output differs.

Usage

```
## S4 method for signature 'omics_array,ANY'
plot(x, y, ...)

## S4 method for signature 'omics_network,ANY'
plot(
  x,
  y,
  choice = "omics_network",
  nv = 0,
  gr = NULL,
  ini = NULL,
  color.vertex = NULL,
  color.edge = NULL,
  video = TRUE,
  weight.node = NULL,
  ani = FALSE,
  size = c(2000, 1000),
  label_v = 1:dim(x@omics_network)[1],
  horiz = TRUE,
  legend.position = "topleft",
  frame.color = "black",
  label.hub = FALSE,
  nround = 2,
  ani.img.name = "Rplot",
  ani.imgdir = "images",
  ani.htmlfile = "index.html",
  outdir,
  ani.group.legend = "Cluster",
  layout = ini,
  alpha = 1,
  pixmap.color = terrain.colors(20),
  ...
)

## S4 method for signature 'omics_predict,ANY'
plot(
  x,
  time = NULL,
```

```
  label_v = NULL,
  frame.color = "white",
  ini = NULL,
  label.hub = FALSE,
  edge.arrow.size = 0.7,
  edge.thickness = 1
)
```

Arguments

x	a omics_array object, a omics_network object or a omics_predict object
y	optional and not used if x is an appropriate structure
...	additional parameters
choice	what graphic should be plotted: either "F" (for a representation of the matrices F) or "network".
nv	the level of cutoff. Defaut to '0'.
gr	a vector giving the group of each gene
ini	using the "position" function, you can fix the position of the nodes.
color.vertex	a vector defining the color of the vertex.
color.edge	color of the edges
video	if ani is TRUE and video is TRUE, the result of the animation is saved as an animated GIF.
weight.node	nodes weighting. Defaults to 'NULL'.
ani	animated plot?
size	vector giving the size of the plot. Default to 'c(2000,1000)'.
label_v	vector defining the vertex labels.
horiz	landscape? Defaults to 'TRUE'.
legend.position	position of the legend.
frame.color	color of the frames.
label.hub	logical ; if TRUE only the hubs are labeled.
nround	number of digits to display
ani.img.name	name of image file for animations
ani.imgdir	name of the image directory for animations
ani.htmlfile	name of the html file for animations
outdir	name of the outdir for animations
ani.group.legend	legend for animations
layout	layout of the graphs
alpha	transparency of the graphs
pixmap.color	color for pixmap graphs

`time` sets the time for plot of the prediction. Defaults to 'NULL'

`edge.arrow.size` size of the arrows ; default to 0.7.

`edge.thickness` edge thickness ; default to 1.

Methods

list("signature(x = \"omics_array\", y = \"ANY\",...)") **x** a omics_array object

list_nv a vector of cutoff at which the network should be shown

list("signature(x = \"omics_network\", y = \"ANY\",...)") **x** a omics_network object

list() Optionnal arguments:

gr a vector giving the group of each gene

choice what graphic should be plotted: either "F" (for a representation of the matrices F) or "network".

nv the level of cutoff. Defaut to 0.

ini using the "position" function, you can fix the position of the nodes

color.vertex a vector defining the color of the vertex

ani vector giving the size of the plot. Default to c(2000,1000). The animation can only be created in the working directory. See the help page of the animation method.

video if ani is TRUE and video is TRUE, the animation result is a GIF video

label_v vector defining the vertex labels

legend.position position of the legend

frame.color color of the frames

label.hub logical ; if TRUE only the hubs are labeled

edge.arrow.size size of the arrows ; default to 0.7

edge.thickness edge thickness ; default to 1.

list("signature(x = \"omics_predict\", y = \"ANY\",...)") **x** a omics_predict object

list() Optional arguments: see plot for omics_network

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
if(require(CascadeData)){
data(micro_US, package="CascadeData")
micro_US<-as.omics_array(micro_US[1:100,],time=c(60,90,210,390),subject=6)
plot(micro_US)
}
```

plotF *Plot functions for the F matrices.*

Description

The graphical output will differ according to the option used.

Usage

```
plotF(x, choice = "Fshape", nround = 2, pixmap.color = terrain.colors(20))
```

Arguments

x	The F matrix.
choice	A string: either "F", "Fpixmap", "Fshape", or "Fshapepixmap"
nround	An integer. For numerical F matrices only. The number of decimal numbers to display.
pixmap.color	For pixmap plots.

Value

Nothing.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
#For numerical/inferred F matrices
plotF(CascadeFinit(4,4),choice="F", nround=1)

if (requireNamespace("pixmap", quietly = TRUE)) {
plotF(CascadeFinit(4,4),choice="Fpixmap")
} else {
plotF(CascadeFinit(4,4),choice="F", nround=1)
}

#For theoritical F matrices
plotF(CascadeFshape(4,4),choice="Fshape")
if (requireNamespace("pixmap", quietly = TRUE)) {
plotF(CascadeFshape(4,4),choice="Fshapepixmap")
} else {
plotF(CascadeFshape(4,4),choice="Fshape")
}
```

position-methods *Returns the position of edges in the network*

Description

Returns the position of edges in the network Retrieve network position for consistent plotting. Utility function to plot networks.

Usage

```
## S4 method for signature 'omics_network'
position(net, nv = 0)
```

Arguments

net	a omics_network object
nv	the level of cutoff at which the analysis should be done

Value

Matrix with as many rows as the number of edges of the network and three columns (name, xcoord, ycoord).

Methods

list("signature(net = \"omics_network\")") Returns a matrix with the position of the node. This matrix can then be used as an argument in the plot function.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(network)
position(network)
```

predict,omics_array-method
Methods for Function predict

Description

Prediction of the gene expressions after a knock-out experience for cascade networks.

Usage

```
## S4 method for signature 'omics_array'
predict(
  object,
  Omega,
  act_time_group = NULL,
  nv = 0,
  targets = NULL,
  adapt = TRUE
)
```

Arguments

object	a omics_array object.
Omega	a omics_network object.
act_time_group	[NULL] vector; at which time the groups (defined by sort(unique(group))) are activated ?
nv	[=0] numeric ; the level of the cutoff
targets	[NULL] vector ; which genes are knocked out ?
adapt	[TRUE] boolean; do not raise an error if used with vectors

Details

The plot of prediction of knock down experiments (i.e. targets<>NULL) is still in beta testing for the moment.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Selection)
data(infos)
pbst_NR4A1 = infos[infos$hgnc_symbol=="NR4A1", "affy_hg_u133_plus_2"]
pbst_EGR1 = infos[infos$hgnc_symbol=="EGR1", "affy_hg_u133_plus_2"]
```

```
gene_IDs = infos[match(Selection@name, infos$affy_hg_u133_plus_), "hgnc_symbol"]

data(networkCascade)
#A nv value can chosen using the cutoff function
nv = .02
NR4A1<-which(is.element(Selection@name,pbst_NR4A1))
EGR1<-which(is.element(Selection@name,pbst_EGR1))
P<-position(networkCascade,nv=nv)

#We predict gene expression modulations within the network if NR4A1 is experimentaly knocked-out.
prediction_ko5_NR4A1<-predict(Selection,networkCascade,nv=nv,targets=NR4A1,act_time_group=1:4)

#Then we plot the results. Here for example we see changes at time points t2, t3 ans t4:
plot(prediction_ko5_NR4A1,time=2:4,ini=P,label_v=gene_IDs)

#We predict gene expression modulations within the network if EGR1 is experimentaly knocked-out.
prediction_ko5_EGR1<-predict(Selection,networkCascade,nv=nv,targets=EGR1,act_time_group=1:4)

#Then we plot the results. Here for example we see changes at time point t2, t3 ans t4:
plot(prediction_ko5_EGR1,time=2:4,ini=P,label_v=gene_IDs)
```

---

probeMerge,omics_array-method

Function to merge probesets

Description

Used to collapse probesets using the collapseRows function of the WGCNA package

Usage

```
## S4 method for signature 'omics_array'
probeMerge(x, ...)
```

Arguments

x	omicsarray
...	Additionnal parameters to the collapseRows function of the WGCNA package

Value

Formal class 'omics_array' [package "Patterns"] with 7 slots

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
if(require(CascadeData)){
data(micro_S)
D<-as.omics_array(micro_S[1:2000,],1:4,6)
D@gene_ID<-jetset::scores.hgu133plus2[D@name,"EntrezID"]
PM <- probeMerge(D)
}
```

`replaceBand` *Replace matrix values by band.*

Description

F matrices utility function.

Usage

```
replaceBand(a, b, k)
```

Arguments

a	The matrix to be replaced
b	The matrix with the replacement values
k	The extend of the replacement: 0 (diagonal only), 1 (diagonal and first extra diagonal), in general an entry is replaced if abs(row(a) - col(a)) <= k

Value

A matrix (same size as a)

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
a=matrix(1:9,3,3)
b=matrix(0,3,3)
replaceBand(a,b,0)
replaceBand(a,b,1)
replaceBand(a,b,2)
```

`replaceDown` *Replace matrix values triangular lower part and by band for the upper part.*

Description

F matrices utility function.

Usage

```
replaceDown(a, b, k)
```

Arguments

a	The matrix to be replaced
b	The matrix with the replacement values
k	The extend of the replacement: 0 (lower part and diagonal only), 1 (lower part and first extra diagonal), in general an entry is replaced if -(row(a) - col(a)) <= k

Value

A matrix (same size as a)

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
a=matrix(1:9,3,3)
b=matrix(1,3,3)
replaceDown(a,b,0)
replaceDown(a,b,1)
replaceDown(a,b,2)
```

`replaceUp` *Replace matrix values triangular upper part and by band for the lower part.*

Description

F matrices utility function.

Usage

```
replaceUp(a, b, k)
```

Arguments

a	The matrix to be replaced
b	The matrix with the replacement values
k	The extend of the replacement: 0 (upper part only), 1 (upper part and first extra diagonal), in general an entry is replaced if (row(a) - col(a)) <= k

Value

A matrix (same size as a)

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
a=matrix(1:9,3,3)
b=matrix(1,3,3)
replaceUp(a,b,0)
replaceUp(a,b,1)
replaceUp(a,b,2)
```

Selection *Selection of genes.*

Description

20 (at most) genes with differential expression at t1, 20 (at most) genes with differential expression at t2, 20 (at most) genes with differential expression at t3, 20 (at most) genes with differential expression at t4 et 20 (at most) genes with global differential expression were selected.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
data(Selection)
head(Selection)
summary(Selection,3)
```

show-methods Show *methods*

Description

Methods for generic function show

Usage

```
## S4 method for signature 'omics_array'
show(object)

## S4 method for signature 'omics_network'
show(object)
```

Arguments

object	an object of class omics-array or omics_network

Methods

list("signature(object = \"ANY\")")

list("signature(object = \"omics_array\")") Print an object of class omics_array

list("signature(object = \"omics_network\")") Print an object of class omics_network

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

summary-methods Summary *methods*

Description

Methods for function summary

Usage

```
## S4 method for signature 'omics_array'
summary(object, nb.graph = NULL, ...)
```

Arguments

object	an object of class omics-array
nb.graph	(optionnal) choose the graph to plot. Displays all graphs by default.
...	additional parameters.

Methods

list("signature(object = \"ANY\")")
list("signature(object = \"omics_array\")") method here~~

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

---

unionOmics-methods *Makes the union between two omics_array objects.*

Description

Makes the union between two omics_array objects.

Usage

```
## S4 method for signature 'omics_array,omics_array'
unionOmics(M1, M2)
```

Arguments

M1	a omics-array or a list of omics-arrays
M2	a omics-array or nothing if M1 is a list of omics-arrays

Methods

list("signature(M1 = \"omics_array\", M2 = \"omics_array\")") Returns a omics_array object which is the union of M1 and M2.

list("signature(M1 = \"list\", M2 = \"ANY\")") Returns a omics_array object which is the union of the elements of M1.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
if(require(CascadeData)){
data(micro_S, package="CascadeData")
#Create another omicsarray object with 100 genes
Mbis<-M<-as.omics_array(micro_S[1:100,],1:4,6)
#Rename the 100 genes
Mbis@name<-paste(M@name,"bis")
rownames(Mbis@omicsarray) <- Mbis@name
#Union (merge without duplicated names) of the two omicsarrays.
str(unionOmics(M,Mbis))
}
```

`unsupervised_clustering,omics_array,numeric,numeric-method`
Cluster a omics_array object: performs the clustering.

Description

Based on soft clustering performed by the Mfuzz package.

Usage

```
## S4 method for signature 'omics_array,numeric,numeric'
unsupervised_clustering(
  M1,
  clust,
  mestim,
  M2 = NULL,
  data_log = TRUE,
  screen = NULL,
  heatmap = TRUE,
  new.window = TRUE
)
```

Arguments

M1	Object of omics_array class.
clust	Number of clusters.
mestim	Fuzzification parameter.
M2	[NULL] Object of omics_array class,
data_log	[TRUE] Should data be logged?
screen	[NULL] Specify ‘mfrow‘ parameter.
heatmap	[TRUE] Plot heatmaps?
new.window	[TRUE] Use new window?

Value

An object of class omics_array with the group slot updated by groups deduced from the soft clustering result.

Author(s)

Bertrand Frederic, Myriam Maumy-Bertrand.

Examples

```
if(require(CascadeData)){
data(micro_S, package="CascadeData")
M<-as.omics_array(micro_S[51:100,],1:4,6)
mc<-unsupervised_clustering_auto_m_c(M)
MwithGrp=unsupervised_clustering(M, 4, mc$m, screen=NULL, heatmap=FALSE, new.window = FALSE)
# Other options
unsupervised_clustering(M, 4, mc$m, screen=c(2,2), heatmap=TRUE, new.window = FALSE)
# Plot the clusters
plot(MwithGrp)
}
```

---

unsupervised_clustering_auto_m_c,omics_array-method

Cluster a omics_array object: determine optimal fuzzification parameter and number of clusters.

Description

Based on soft clustering performed by the Mfuzz package.

Usage

```
## S4 method for signature 'omics_array'
unsupervised_clustering_auto_m_c(
  M1,
  clust = NULL,
  mestim = NULL,
  M2 = NULL,
  data_log = TRUE,
  screen = NULL,
  crange = NULL,
  repeats = NULL,
  cselect = TRUE,
  dminimum = FALSE
)
```

Arguments

M1	Object of omics_array class.
clust	[NULL] Number of clusters.
mestim	[NULL] Fuzzification parameter.
M2	[NULL] Object of omics_array class,
data_log	[TRUE] Should data be logged?
screen	[NULL] Specify ‘screen‘ parameter.

crange	[NULL] Specify ‘crange‘ parameter.
repeats	[NULL] Specify ‘repeats‘ parameter.
cselect	[TRUE] Estimate ‘cselect‘ parameter.
dminimum	[FALSE] Estimate ‘dminimum‘ parameter.

Value

m	Estimate of the optimal fuzzification parameter.
c	Estimate of the optimal number of clusters.
csearch	More result from the cselection function of the Mfuzz package

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Examples

```
if(require(CascadeData)){
data(micro_S, package="CascadeData")
M<-as.omics_array(micro_S[1:100,],1:4,6)
mc<-unsupervised_clustering_auto_m_c(M)
}
```

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