

# Package ‘Cascade’

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Cascade-package	<i>The Cascade Package: Selection, Reverse-Engineering and Prediction in Cascade Networks</i>
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### Description

A modeling tool allowing gene selection, reverse engineering, and prediction in cascade networks.  
 Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014) <doi:10.1093/bioinformatics/btt705>.

### Author(s)

This package has been written by Frédéric Bertrand, Myriam Maumy-Bertrand and Nicolas Jung with biological insights from Laurent Vallat. Maintainer: Frédéric Bertrand <frederic.bertrand@math.unistra.fr>

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

---

analyze\_network, network-method  
*Analysing the network*

---

**Description**

Calculates some indicators for each node in the network.

**Usage**

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

**Arguments**

Omega	a network object
nv	the level of cutoff at which the analysis should be done
label_v	(optional) the name of the genes

**Value**

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

**Author(s)**

Nicolas Jung, Frédéric Bertrand, Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

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

---

as.micro_array	<i>Coerce a matrix into a micro_array object.</i>
----------------	---------------------------------------------------

---

**Description**

Coerce a matrix into a micro\_array object.

**Usage**

```
as.micro_array(M, time, subject)
```

**Arguments**

M	A matrix. Contains the microarray measurements. Should 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 individuals. This matrix should be created using <code>cbind(M1,M2,...)</code> with $M1$ a $N*T$ matrix with the measurements for individual 1, $M2$ a $N*T$ matrix with the measurements for individual 2.
time	A vector. The time points measurements.
subject	The number of subjects.

**Value**

A micro\_array object.

**Author(s)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```

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

```

---

compare-methods	<i>Some basic criteria of comparison between actual and inferred network.</i>
-----------------	-------------------------------------------------------------------------------

---

**Description**

Allows comparison between actual and inferred network.

**Usage**

```

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

```

**Arguments**

Net	A network object containing the actual network.
Net_inf	A 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 : sensibility, predictive positive value, and the F-score

**Methods**

```
list("signature(Net = \"network\", Net_inf = \"network\", nv = \"numeric\")")
```

**Author(s)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```

data(Net)
data(Net_inf)

#Comparing true and inferred networks
F_score=NULL

#Here are the cutoff level tested
test.seq<-seq(0,max(abs(Net_inf@network*0.9)),length.out=200)
for(u in test.seq){
F_score<-rbind(F_score,Cascade::compare(Net,Net_inf,u))
}
matplot(test.seq,F_score,type="l",ylab="criterion value",xlab="cutoff level",lwd=2)

```

---

cutoff, network-method *Choose the best cutoff*

---

**Description**

Allows estimating the best cutoff, in function of the scale-freeness of the network. For a sequence of cutoff, the corresponding p-value is then calculated.

**Usage**

```

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

```

**Arguments**

Omega	a network object
sequence	(optional) a vector corresponding to the sequence of cutoffs that will be tested.
x_min	(optional) 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)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

## References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

## Examples

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

---

dim	<i>Dimension of the data</i>
-----	------------------------------

---

## Description

Dimension of the data

## Usage

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

## Arguments

x                    an object of class "micro-array"

## Methods

**list("signature(x = \"micro\_array\")")** Gives the dimension of the matrix of measurements.

## Examples

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

---

 evolution, network-method

*See the evolution of the network with change of cutoff*


---

### Description

See the evolution of the network with change of cutoff. This function may be usefull to see if the global topology is changed while increasing the cutoff.

### Usage

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

### Arguments

net	a network object
list_nv	a vector of cutoff at which the network should be shown
gr	a vector giving the group of each gene
color.vertex	a vector giving the color of each node
fix	logical, should the position of the node in the network be calculated once at the beginning ? Defaults to TRUE.
gif	logical, TRUE
taille	vector giving the size of the plot. Default to c(2000,1000)
label_v	(optional) the name of the genes
legend.position	(optional) the position of the legend, defaults to "topleft"
frame.color	(optional) the color of the frame, defaults to "black"
label.hub	(optional) boolean, defaults to FALSE

### Value

A HTML page with the evolution of the network.



**Author(s)**

Nicolas Jung, Frédéric Bertrand, Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```
data(network)
sequence<-seq(0,0.2,length.out=20)
#setwd("inst/animation")
#evolution(network,sequence)
```

---

geneNeighborhood, network-method

*Find the neighborhood of a set of nodes.*

---

**Description**

Find the neighborhood of a set of nodes.

**Usage**

```
## S4 method for signature '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 = FALSE
)
```

**Arguments**

net	a network object
targets	a vector containing the set of nodes
nv	the level of cutoff. Default to 0.
order	of the neighborhood. Default 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)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```
data(Selection)
data(network)
#A nv value can chosen using the cutoff function
nv=.11
EGR1<-which(match(Selection@name,"EGR1")==1)
P<-position(network,nv=nv)

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

---

geneSelection	<i>Methods for selecting genes</i>
---------------	------------------------------------

---

**Description**

Selection of differentially expressed genes.

**Usage**

```
## S4 method for signature 'micro_array,micro_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
)

## S4 method for signature 'micro_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 <code>micro_array</code> object or a list of <code>micro_array</code> objects. In the first case, the <code>micro_array</code> 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 <code>micro_array</code> object or a list of strings. In the first case, the <code>micro_array</code> object represents the stimulated measurements. In the second case, the list is the way to specify the contrast: <b>First element:</b> 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. <b>Second element:</b> 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 through time, the option <code>cont=TRUE</code> should be used. <b>Third element:</b> 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 <code>tot.number &lt; 0</code> all differentially genes are selected. If <code>tot.number &gt; 1</code> , <code>tot.number</code> is the maximum of differentially genes that will be selected. If <code>0 &lt; tot.number &lt; 1</code> , <code>tot.number</code> represents the proportion of differentially genes that are selected.
data_log	logical (default to TRUE); should data be logged ?
wanted.patterns	a matrix with wanted patterns [only for <code>geneSelection</code> ].
forbidden.patterns	a matrix with forbidden patterns [only for <code>geneSelection</code> ].
peak	integer. At which time points measurements should the genes be selected [optional for <code>geneSelection</code> ].
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.
durPeak	vector of size 2 (default to <code>c(1,1)</code> ); the first elements gives the length of the peak at the left, the second at the right. [only for <code>genePeakSelection</code> ]
abs_val	logical (default to TRUE); should genes be selected on the basis of their absolute value expression ? [only for <code>genePeakSelection</code> ]
alpha_diff	float; the risk level

**Value**

A micro\_array object.

**Author(s)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```

  if(require(CascadeData)){
data(micro_US)
micro_US<-as.micro_array(micro_US,time=c(60,90,210,390),subject=6)
data(micro_S)
micro_S<-as.micro_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.micro_array(micro_US,time=c(60,90,210,390),subject=6)
data(micro_S)
micro_S<-as.micro_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<-unionMicro(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, network-method

*Simulates microarray data based on a given network.*

---

## Description

Simulates microarray data based on a given network.

## Usage

```

## S4 method for signature 'network'
gene_expr_simulation(network, time_label = 1:4, subject = 5, level_peak = 100)

```

**Arguments**

network	A network object.
time_label	a vector containing the time labels.
subject	the number of subjects
level_peak	the mean level of peaks.

**Value**

A micro\_array object.

**Author(s)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, bt705.

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*, 110(2), 459-464.

**Examples**

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

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

---

head,micro\_array-method

*Overview of a micro\_array object*

---

**Description**

Overview of a micro\_array object.

**Usage**

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

**Arguments**

```
x          an object of class 'micro_array'.
...        additional parameters
```

**Methods**

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

**Examples**

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

---

inference,micro\_array-method

*Reverse-engineer the network*

---

**Description**

Reverse-engineer the network.

**Usage**

```
## S4 method for signature 'micro_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"
)
```



**Arguments**

M	a micro_array object.
tour.max	maximal number of steps. Defaults to 'tour.max=30'
g	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	convergence criterion. Defaults to 'conv=10e-3'
cv.subjects	should the cross validation be done removing the subject one by one ? Defaults to 'cv.subjects=TRUE'.
nb.folds	Relevant only if cv.subjects is FALSE. The number of folds in cross validation. Defaults to 'NULL'.
eps	machine zero. Defaults to '10e-5'.
type.inf	"iterative" or "noniterative" : should the algorithm be computed iteratively. Defaults to "iterative".

**Value**

A network object.

**Author(s)**

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

**References**

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

**Examples**

```
#With simulated data
data(M)
infM <- inference(M)
str(infM)

#With selection of genes from GSE39411
data(Selection)
infSel <- inference(Selection)
str(infSel)
```

M *Simulated M data for examples.*

---

**Description**

Simulated M microarray.

**Examples**

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

---

micropredict-class *Class "micropredict"*

---

**Description**

The "micropredict" class

**Objects from the Class**

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

**Examples**

```
showClass("micropredict")
```

---

micro\_array-class *Class "micro\_array"*

---

**Description**

The "micro\_array" class

**Objects from the Class**

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

**Examples**

```
showClass("micro_array")
```

---

Net	<i>Simulated network data for examples.</i>
-----	---------------------------------------------

---

**Description**

Simulated network.

**Examples**

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

---

network	<i>A network object data.</i>
---------	-------------------------------

---

**Description**

A network object. It is the same as the result in the vignette for the inference of the network.

**Examples**

```
data(network)
plot(network)
print(network)
```

---

network-class	<i>Class "network"</i>
---------------	------------------------

---

**Description**

The "network" class

**Objects from the Class**

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

**Examples**

```
showClass("network")
```

---

network_random	<i>Generates a network.</i>
----------------	-----------------------------

---

### 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 network object.

### Author(s)

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

## References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

## 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

*Reverse-engineered network of the simulated data.*

---

## Description

The reverse-engineered network of the simulated data (M and Net).

## Examples

```
data(Net_inf)
str(Net_inf)
```

---

plot-methods

*Plot*

---

## Description

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

**Usage**

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

```
## S4 method for signature 'network,ANY'
plot(
  x,
  y,
  choice = "network",
  nv = 0,
  gr = NULL,
  ini = NULL,
  color.vertex = NULL,
  video = TRUE,
  weight.node = NULL,
  ani = FALSE,
  taille = c(2000, 1000),
  label_v = 1:dim(x@network)[1],
  horiz = TRUE,
  legend.position = "topleft",
  frame.color = "black",
  label.hub = FALSE,
  ...
)
```

```
## S4 method for signature 'micropredict,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 micro_array object, a network object or a micropredict 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. Default to '0'.
gr	a vector giving the group of each gene
ini	using the "position" function, you can fix the position of the nodes.

<code>color.vertex</code>	a vector defining the color of the vertex.
<code>video</code>	if <code>ani</code> is TRUE and <code>video</code> is TRUE, the result of the animation is saved as an animated GIF.
<code>weight.node</code>	nodes weighting. Defaults to 'NULL'.
<code>ani</code>	animated plot?
<code>taille</code>	vector giving the size of the plot. Default to 'c(2000,1000)'.
<code>label_v</code>	vector defining the vertex labels.
<code>horiz</code>	landscape? Defaults to 'TRUE'.
<code>legend.position</code>	position of the legend.
<code>frame.color</code>	color of the frames.
<code>label.hub</code>	logical ; if TRUE only the hubs are labeled.
<code>time</code>	sets the time for plot of the prediction. Defaults to 'NULL'
<code>edge.arrow.size</code>	size of the arrows ; default to 0.7.
<code>edge.thickness</code>	edge thickness ; default to 1.

## Methods

**list("signature(x = \"micro\_array\", y = \"ANY\",...))** `x` a micro\_array object

**list\_nv** a vector of cutoff at which the network should be shown

**list("signature(x = \"network\", y = \"ANY\",...))** `x` a 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. Default 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** animated plot?

**size** vector giving the size of the plot. Default to c(2000,1000)

**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 = \"micropredict\", y = \"ANY\",...))** `x` a micropredict object

**list()** Optionnal arguments: see plot for network

**Examples**

```
data(Net)
plot(Net)
```

```
data(M)
plot(M)
```

```
data(Selection)
data(network)
nv<-0.11
plot(network,choice="network",gr=Selection@group,nv=nv,label_v=Selection@name,
edge.arrow.size=0.9,edge.thickness=1.5)
```

---

position-methods	<i>Returns the position of edges in the network</i>
------------------	-----------------------------------------------------

---

**Description**

Returns the position of edges in the network

**Usage**

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

**Arguments**

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

**Methods**

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

**Examples**

```
data(Net)
position(Net)
```



---

```
predict,micro_array-method
    Prediction of the gene expressions after a knock-out experience
predict
```

---

## Description

Prediction of the gene expressions after a knock-out experience

## Usage

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

## Arguments

object	a micro_array object
Omega	a network object.
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 instead of one column matrices.

## Author(s)

Nicolas Jung, Frédéric Bertrand , Myriam Maumy-Bertrand.

## References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2014). Cascade: a R-package to study, predict and simulate the diffusion of a signal through a temporal gene network. *Bioinformatics*, btt705.

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*, 110(2), 459-464.

## Examples

```
data(Selection)
data(network)
#A nv value can chosen using the cutoff function
nv=.11
EGR1<-which(match(Selection$name,"EGR1")==1)
P<-position(network,nv=nv)

#We predict gene expression modulations within the network if EGR1 is experimentally knocked-out.
prediction_ko5<-predict(Selection,network,nv=nv,targets=EGR1)
```

```
#Then we plot the results. Here for example we see changes at time point t2:
plot(prediction_ko5,time=2,ini=P,label_v=Selection@name)
```

---

```
print-methods          Methods for Function print
```

---

### Description

Methods for function print

### Usage

```
## S4 method for signature 'micro_array'
print(x, ...)

## S4 method for signature 'network'
print(x, ...)
```

### Arguments

```
x          an object of class micro-array or network
...        additional parameters
```

### Examples

```
data(Net)
print(Net)

data(M)
print(M)
```

---

```
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.

### Examples

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

---

summary-methods      *Methods for Function summary*

---

**Description**

Methods for function summary

**Usage**

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

**Arguments**

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

**Examples**

```
data(M)
summary(M)
```

---

unionMicro-methods      *Makes the union between two micro\_array objects.*

---

**Description**

Makes the union between two micro\_array objects.

**Usage**

```
## S4 method for signature 'micro_array,micro_array'
unionMicro(M1, M2)
```

**Arguments**

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

**Methods**

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

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

**Examples**

```
data(M)
#Create another microarray object with 100 genes
Mbis<-M
#Rename the 100 genes
Mbis@name<-paste(M@name,"bis")
rownames(Mbis@microarray) <- Mbis@name
#Union (merge without duplicated names) of the two microarrays.
str(unionMicro(M,Mbis))
```

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