

Package ‘Cascade’

March 24, 2014

Type Package

Title Selection, Reverse-Engineering and Prediction in Cascade networks.

Version 1.03

Date 2014-03-24

Author Nicolas Jung, Frederic Bertrand, Myriam Maumy-Bertrand Laurent Vallat

Maintainer <cascade@math.unistra.fr>

Description

The Cascade is a modeling tool allowing gene selection, reverse engineering, and prediction.

License GPL (>= 2)

Depends methods, abind, animation, cluster, graphics, grDevices, grid,igraph, lars, lattice, limma, magic, methods, nnls, splines,stats, stats4, survival, tnet, utils, VGAM

Collate global.R micro_array.R network.R micro_array-network.R micropredict.R

R topics documented:

Cascade-package	1
analyze_network	2
as.micro_array	3
compare	4
cutoff	5
dim	6
evolution	6
geneNeighborhood	7
genePeakSelection	8
gene_expr_simulation	9
head	10
inference	10
micropredict-class	11
micro_array-class	12

micro_S	13
micro_US	13
network	14
network-class	14
network_random	15
plot-methods	16
position-methods	17
predict	17
print-methods	17
summary-methods	18
unionMicro-methods	18

Cascade-package *The Cascade Package*

Description

The Cascade is a modeling tool allowing gene selection, reverse engineering, and prediction.

Details

Package: Cascade
 Type: Package
 Version: 1.03
 Date: 2014-03-24
 License: GNU 2.0
 Depends: methods

Author(s)

This package has been written by Nicolas Jung in collaboration with Frederic Bertrand, Myriam Maumy-Bertrand and Laurent Vallat. Maintainer: <cascade@math.unistra.fr>

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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 *Analysing the network*

Description

Calculates some indicators for each node in the network.

Usage

```
analyze_network (Omega, nv, ...)
```

Arguments

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

Value

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

Author(s)

Nicolas Jung, Fr ed eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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 *Coerce a matrix into a micro_array object.*

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, Fr ed eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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(micro_US)
micro_US<-as.micro_array(micro_US,time=c(60,90,210,390),subject=6)
```

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

Description

Allows comparison between actual and inferred network.

Usage

```
compare(Net, Net_inf, nv)
```

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

Author(s)

Nicolas Jung, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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.

cutoff	<i>Choose the best cutoff</i>
--------	-------------------------------

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

```
cutoff(Omega, ...)
```

Arguments

Omega a network object
 . . . Optional arguments:
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)

Nicolas Jung, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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

Methods

signature(x = "micro_array") Gives the dimension of the matrix of measurements.

`evolution`*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

```
evolution(net, list_nv, ...)
```

Arguments

<code>net</code>	a network object
<code>list_nv</code>	a vector of cutoff at which the network should be shown
<code>...</code>	Optionnal arguments: 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 ? Default to TRUE. taille vector giving the size of the plot. Default to c(2000,1000) <code>...</code> see plot function

Value

A HTML page with the evolution of the network.

Author(s)

Nicolas Jung, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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)
evolution(network,sequence)
```

geneNeighborhood *Find the neighborhood of a set of nodes.*

Description

Find the neighborhood of a set of nodes.

Usage

```
geneNeighborhood(net, targets, ...)
```

Arguments

net	a network object
targets	a vector containing the set of nodes
...	Optional arguments. See plot options.

Value

The neighborhood of the targeted genes.

Author(s)

Nicolas Jung, Fr ed eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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

```
#See vignette
```

genePeakSelection *Methods for selecting genes*

Description

Selection of differentially expressed genes.

Usage

```
geneSelection(x, y, tot.number, ...)
genePeakSelection(x, pic, ...)
```

Arguments

- | | |
|------------|---|
| x | either a micro_array object or a list of micro_array objects. In the first case, the micro_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 micro_array object or a list of strings. In the first case, the micro_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 through time, the option cont=TRUE should be used.
Third element: depends on the first element. It is not 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 differentially genes that will be selected. If 0 < tot.number < 1, tot.number represents the proportion of differentially genes that are selected. |
| pic | integer. At which time points measurements should the genes be selected [optional for geneSelection]. |
| ... | Optional arguments:
M2 a micro_array object. The unstimulated measurements.
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].
durPic vector of size 2 (default to c(1,1)) ; the first elements gives the length of the pic 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 micro_array object.

Author(s)

Nicolas Jung, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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.

gene_expr_simulation

Simulates microarray data based on a given network.

Description

Simulates microarray data based on a given network.

Usage

```
gene_expr_simulation(network, ...)
```

Arguments

network A network object.
... **time_label** a vector containing the time labels.
subject the number of subjects
level_pic the mean level of pics.

Value

A micro_array object.

Author(s)

Nicolas Jung, Fr\'ed\'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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

```
#See vignette
```

head	<i>Overview of a micro_array object</i>
------	---

Description

Overview of a micro_array object.

Methods

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

signature(x = "micro_array") Gives an overview.

inference	<i>Reverse-engineer the network</i>
-----------	-------------------------------------

Description

Reverse-engineer the network.

Usage

```
inference(M, ...)
```

Arguments

M a micro_array object.
 . . . Optional arguments:
tour.max=30 maximal number of steps.
g=function(x) 1/x the new solution is chosen as (the old solution + g(x) * the new solution)/(1+g(x)) where x is the number of steps.
conv=10e-3 convergence criterion.
cv.subjects=TRUE should the cross validation be done removing the subject one by one ?
nb.folds=NULL Relevant only if cv.subjects is FALSE. The number of folds in cross validation.
eps=10e-5 machine zero
type.inf="iterative" "iterative" or "noniterative" : should the algorithm be computed iteratively

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. (2013). 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(micro_US)
#inference(micro_US)
#See vignette for more details
```

micropredict-class *Class* "micropred"

Description

2254

Objects from the Class

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

Examples

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

```
micro_array-class  Class "micro_array"
```

Description

The Class

Objects from the Class

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

Slots

```
microarray: Object of class "matrix" ~~
name: Object of class "vector" ~~
group: Object of class "vector" ~~
start_time: Object of class "vector" ~~
time: Object of class "vector" ~~
subject: Object of class "numeric" ~~
```

Methods

```
dim signature(x = "micro_array"):...
genePicSelection signature(M1 = "micro_array", M2 = "micro_array", pic = "numeric"):
...
geneSelection signature(x = "micro_array", y = "micro_array", tot.number = "numeric"):
...
geneSelection signature(x = "list", y = "list", tot.number = "numeric"):
...
head signature(x = "micro_array"):...
inference signature(M = "micro_array"):...
plot signature(x = "micro_array", y = "ANY"):...
plot signature(x = "micro_array", y = "ANY"):...
plot signature(x = "micropredict", y = "ANY"):...
predict signature(object = "micro_array"):...
print signature(x = "micro_array"):...
summary signature(object = "micro_array"):...
unionMicro signature(M1 = "micro_array", M2 = "micro_array"):...
```

Examples

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

micro_S	<i>Stimulated data</i>
---------	------------------------

Description

Stimulated data

Usage

```
data(micro_S)
```

Format

A data frame with 54613 probesets measured 6 times through 4 time points.

References

Vallat, L., Park, Y., Li, C., & Gribben, J. G. (2007). Temporal genetic program following B-cell receptor cross-linking: altered balance between proliferation and death in healthy and malignant B cells. *Blood*, 109(9), 3989-3997. 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(micro_S)
```

micro_US	<i>Unstimulated data</i>
----------	--------------------------

Description

Unstimulated data

Usage

```
data(micro_US)
```

Format

A data frame with 54613 probesets measured 6 times through 4 time points.

References

Vallat, L., Park, Y., Li, C., & Gribben, J. G. (2007). Temporal genetic program following B-cell receptor cross-linking: altered balance between proliferation and death in healthy and malignant B cells. *Blood*, 109(9), 3989-3997. 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(micro_US)
```

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

Description

A network object (the same as the result in the vignette).

Usage

```
data(network)
```

Examples

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

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

Description

2254

Objects from the Class

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

Slots

network: Object of class "matrix" ~~
name: Object of class "vector" ~~
F: Object of class "array" ~~
convF: Object of class "matrix" ~~
convO: Object of class "vector" ~~
time_pt: Object of class "vector" ~~

Methods

analyze_network signature(Omega = "network"): ...
cutoff signature(Omega = "network"): ...
evolution signature(net = "network"): ...
geneNeighborhood signature(net = "network"): ...
plot signature(x = "network", y = "ANY"): ...
plot signature(x = "network", y = "micro_array"): ...
position signature(net = "network"): ...
print signature(x = "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, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

References

Jung, N., Bertrand, F., Bahram, S., Vallat, L., and Maumy-Bertrand, M. (2013). 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.

plot-methods

Plot

Description

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

Methods

signature(x = "micro_array", y = "ANY", ...) **x** a micro_array object

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

signature(x = "network", y = "ANY", ...) **x** a network object

... 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 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.

signature(x = "micropredict", y = "ANY", ...) **x** a micropredict object

... Optionnal arguments: see plot for network

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

Description

Returns the position of edges in the network

Methods

`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.

predict *Prediction of the gene expressions after a knock-out experience*
predict

Description

Prediction of the gene expressions after a knock-out experience

Usage

`predict(object, ...)`

Arguments

`object` a micro_array object
`...` Other arguments:
Omega a network object.
nv [=0] numeric ; the level of the cutoff
targets [NULL] vector ; which genes are knocked out ?

Author(s)

Nicolas Jung, Fr'ed'eric Bertrand , Myriam Maumy-Bertrand.

print-methods *~~ Methods for Function print ~~*

Description

Methods for function `print` ~~

summary-methods *Methods for Function summary*

Description

Methods for function summary

unionMicro-methods *Makes the union between two micro_array objects.*

Description

Makes the union between two micro_array objects.

Methods

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

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