Package ‘simPATHy’

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Type Package
Title A Method for Simulating Data from Perturbed Biological Pathways
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Description Simulate data from a Gaussian graphical model or a Gaussian Bayesian network in two conditions. Given a covariance matrix of a reference condition simulate plausible disregulations.
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chimera

Description

A matrix containing the expression values of 3405 genes deriving from Affimetrix single channel technology, consisting of 41 observations from one experimental condition (absence of BCR/ABL gene arrangement, class 1), and 37 observations from another experimental condition (presence of BCR/ABL gene arrangement, class 2).

Usage

chimera

Format

A matrix with 8405 genes (rows) and 78 samples (columns).

Source


Examples

data(chimera)
easyLookDys

Dysregulation summary

Description
Summary of the result for a quick look of simPATHy function.

Usage
easyLookDys(resObj, digits = 4)

Arguments
- resObj: The output of simPATHy function (simPATHy class object).
- digits: Integer indicating the number of decimal places to be used.

Value
Nice formatted output of simPATHy dysregulation
Nicely formatted output of simPATHy dysregulation.

easyLookShiny
Visual dysregulation summary

Description
A Shiny application for visual summary of dysregulation.

Usage
easyLookShiny(resObj, graph, heightGraph = NULL, heightMatrix = NULL)

Arguments
- resObj: The output of simPATHy function
- graph: The graphNEL object given to the simPATHy function to obtain resObj.
- heightGraph, heightMatrix: The height of the graph and correlation matrix plots in pixels. Must be a number, which will be coerced to a string and have `px` append.

Value
Interactive plots for exploring the output of simPATHy.

See Also
- simPATHy, plotGraphNELD3, plotCorGraph, easyLookDys
fitSgraph

Estimate covariance matrix of a graphical model

Description

Fit a Gaussian Graphical Model or a Gaussian Bayesian Network by maximum likelihood.

Usage

fitSgraph(graph, S)

Arguments

graph A directed or undirected graph represented as a graphNEL object.
S A sample covariance matrix

Details

If graph is undirected it uses the Iterative Proportionional Fitting algorithm (qpgraph package). If graph is directed it uses Iterative Conditional Fitting (ggm package).

Value

A covariance matrix with the independence constraints entailed by the graph.

References


See Also

icfmag, qpIPF
generatePath

Find one path in a graph

Description
Find one shortest path in the graph between two given nodes.

Usage
generatePath(graph, from = NULL, to = NULL)

Arguments
- graph: A directed or undirected graph represented as a graphNEL object.
- from, to: The nodes (character node id) giving the first and the last nodes of the path to be calculated. If NULL then the from and to nodes are randomly choosen.

Value
A list of edges in edgesList format (see gRbase).

See Also
get.all.shortest.paths

getPathShiny

Choose a path in a graph from an interactive shiny app

Description
Choose a path in a graph from an interactive shiny app with the rigth format for simPATHy function.

Usage
generatePath(graph)

Arguments
- graph: A graphNEL object.

Value
Selected path with the rigth format for simPATHy function.

See Also
simPATHy
Examples

```r
if(require(gRbase)){
  graph <- gRbase::dag(~c:a, ~c:b, ~d:c, ~e:d)

  # Launch the interactive plot
  # path <- getPathShiny(graph)
}
```

**graphNELD3-shiny**  
*Shiny bindings for plotGraphNELD3*

**Description**

Output and render functions for using plotGraphNELD3 within Shiny applications and interactive Rmd documents.

**Usage**

```r
graphNELD3Output(outputId, width = "100\%", height = "400px")
renderGraphNELD3(expr, env = parent.frame(), quoted = FALSE)
```

**Arguments**

- `outputId`  
  Output variable to read from

- `width`, `height`  
  Must be a valid CSS unit (like '100\%', '400px', 'auto') or a number, which will be coerced to a string and have 'px' appended.

- `expr`  
  An expression that generates a graphNELD3

- `env`  
  The environment in which to evaluate expr.

- `quoted`  
  Is expr a quoted expression (with `quote()`)? This is useful if you want to save an expression in a variable.

**makePositiveDefinite**  
*Positive definite matrix*

**Description**

Adjust the diagonal of a symmetric square matrix, by the smallest eigenvalue method, in order to make it positive definite.

**Usage**

```r
makePositiveDefinite(M1, M2 = NULL, threshold = 0.1)
```
Arguments

M1, M2
A squared numeric matrix, typically a correlation or a covariance matrix. It must be symmetric.

threshold
A correction factor.

Details

Finds the smallest eigenvalue lambda of M1 (or M1 and M2 if supplied) and adds (threshold-lambda) to the diagonal to make it positive definite.

Value

A list with the corrected input matrices and the correction threshold-lambda.

plotCorGraph

Plot correlation or partial correlation matrix

Description

Plot a correlation or partial correlation matrix with the possibility to emphasize the graphical structure.

Usage

plotCorGraph(  
  S1,  
  type = "cor",  
  S2 = NULL,  
  graph = NULL,  
  path = NULL,  
  main = "",  
  colLim = c(-1, 1),  
  legendColor = TRUE  
)

Arguments

S1, S2
Sample covariance matrix. If S2 supplied, the difference between the two corresponding correlation or partial correlation matrices is plotted.

type
Character string specifying which matrix is to be plotted. Either cor for correlation matrix, or pcor for partial correlation matrix.

graph
A graphNEL object.

path
A list of edges in edgesList format (see gRbase).

main
The main title.

colLim
Numeric vector of length two specifying the lower and upper bound of the color range (see Details).

legendColor
Logical value indicating whether the color legend should be added to the plot.
Details

If the graph is supplied, the zero elements of the adjacency matrix are represented as shaded squares, whereas non-zero elements are represented as squares with grey borderline.

Admissible values for colLim are contained in the interval \([-1,1]\) when S2=\texttt{NULL}, otherwise the admissible interval is \([-2,2]\). When an element is outside of the colLim interval, it is colored gray.

Value

Correlation or partial correlation matrix plot.

Examples

```r
if( require(gRbase) & require(graph)){
  graph <- gRbase::ug(~a:b, ~a:c, ~c:d, ~b:d, ~b:c)

  S <- matrix(c(2, 0.8,0.5,-0.3,
               0.8,1.5,0.6,-0.7,
               0.5,0.6,1, 0.7,
               -0.3,-0.7,0.7,3), ncol=4,nrow=4)
  colnames(S) <- rownames(S) <- graph::nodes(graph)

  # Plot the correlation matrix of S
  plotCorGraph(S)

  S<-fitSgraph(graph = graph,S = S)
  # Change the color range
  plotCorGraph(S, colLim=c(-0.5,0.5))

  # Visualize the adjacency matrix
  plotCorGraph(S, type="cor", graph = graph)

  # Show the partial correlation matrix
  plotCorGraph(S, type="pcor", graph = graph)

  # Plot the difference between two matrices
  S2 <- S
  # Change the element c~a
  S2["a","c"] <- S2["c","a"]<- -0.1
  plotCorGraph(S1=S, S2=S2)
  plotCorGraph(S1=S, S2=S2, type="pcor")

  S2<-fitSgraph(graph = graph,S = S2)
  # Highlight the graphical structure
  plotCorGraph(S1=S, S2=S2, type="pcor",graph = graph)
  # Highlight the element c~a
  plotCorGraph(S1=S, S2=S2, type="pcor",graph = graph,path = list(\(c("a","c")\)))
}
```
Description

Dynamic plot of a graphNEL object with the possibility to emphasize the strength of relations between nodes, represented by either a pairwise correlation or a partial correlation coefficient.

The interactive graph is an implementation of the javascript D3.js package (force-layout) for undirected and directed graphNEL objects (see references).

Usage

```r
plotGraphNELD3(
  graph,
  type = "cor",
  S1 = NULL,
  S2 = NULL,
  colLim = c(-1, 1),
  legendColor = TRUE,
  colNode = "#c0c0c0"
)
```

Arguments

- **graph**: A graphNEL object.
- **type**: Character string specifying which matrix is to be used. Either cor for correlation matrix, or pcor for partial correlation matrix.
- **S1, S2**: Sample covariance matrix. If S1 is supplied edges between nodes are colored in accordance with pairwise correlation or partial correlation coefficients. If S2 supplied, the difference between the two corresponding correlation or partial correlation matrices is plotted.
- **colLim**: Numeric vector of length two specifying the lower and upper bound of the color range (see Details).
- **legendColor**: Logical value indicating whether the color legend should be added to the plot.
- **colNode**: A character string specifying the colour of the nodes. The colour node is common for all nodes.

Details

Admissible values for colLim are contained in the interval [-1, 1] when S2=NULL, otherwise the admissible interval is [-2, 2]. When an element is outside of the colLim interval, it is colored gray and represented as a dashed link.

Value

Dynamic plot of a graphNEL object.
References

https://d3js.org (Micheal Bostock).
https://christophergandrud.github.io/networkD3/ (Christopher Gandrud, JJ Allaire, & Kent Russell)

Examples

if(require(gRbase) & require(graph)){
  graph <- gRbase::ug(~a:b, ~a:c, ~c:d, ~b:d, ~b:c)
  # Plot a graphNEL
  plotGraphNELD3(graph)

  # Plot a graphNEL coloring edges in correspondence with pairwise correlation coefficients
  S <- matrix(c(2, 0.8, 0.5, -0.3,
                0.8, 1.5, 0.6, -0.7,
                0.5, 0.6, 1, 0.7,
                -0.3, -0.7, 0.7, 3), ncol=4, nrow=4)
  colnames(S) <- rownames(S) <- graph::nodes(graph)
  plotGraphNELD3(graph, S1=S)

  # Plot a graphNEL coloring edges in correspondence with partial correlation coefficients
  plotGraphNELD3(graph, S1=S, type="pcor")

  # Change the color range
  plotGraphNELD3(graph, S1=S, type="cor", colLim=c(-0.7, 0.8))

  # Change nodes color
  plotGraphNELD3(graph, S1=S, type="cor", colNode = "pink")

  # Plot the difference between two graphical models
  S2 <- S
  S2[1, 3] <- S2[3, 1] <- -0.1
  plotGraphNELD3(graph, S1=S, S2=S2)
}

simPATHy

Simulate data from a graphical model

Description

Simulate data in two different conditions with a common structure of dependences. The two different conditions are characterized by different strengths of the links between nodes (dysregulation).

Usage

simPATHy(
  graph,
path = NULL,
S = NULL,
min = 2,
max = 3,
prob = 1,
n1 = 500,
n2 = n1,
digits = 5,
mu1 = 0,
mu2 = mu1,
muRandom = FALSE
)

Arguments

graph          A graphNEL object.
path           A list of edges in edgesList format (see gRbase).
S              The sample covariance matrix.
min, max       Vectors of length 1 or of the same length as path containing the lower and upper
                limits of a uniform distribution. The strength of dysregulation is sampled
                uniformly from the interval [min, max]: a value smaller than 1 represents deac-
                tivation, a value greater than 1 represents activation. If path=NULL only the first
                element is used.
prob           A vector of size 1 or of the same length as path, giving the probability to change
                the sign of the correlation coefficient for each edge. prob=0 implying that the
                sign of the dysregulation should be changed, and prob=1 implying that the sign
                should be left unaltered (default). Values between these two extremes allow for
                random sign switch: the sign is changed with probability 1-prob.
n1, n2         Number of observations to generate from the two conditions.
digits         Integer indicating the number of decimal places to be used.
mu1, mu2       A vector of size 1 or of the length equal to the number of nodes in the graph.
                Means of the multivariate normal distributions from which observations are gen-
                erated. If mu1 (and/or mu2) is a vector it has to be named in accordance with the
                names of the nodes of the graph.
muRandom       Logical. If muRandom=TRUE the means of the variables are randomly generated.

Details

If the matrix S does not reflect conditional independence constraints imposed by the graph simPATHy
uses the maximum likelihood estimation of covariance matrices for graphical models via internal function
fitSgraph.

When the dysregulation of the initial (reference condition) covariance matrix leads to a matrix that is
no longer positive definite, the resulting matrix is corrected via internal function makePositiveDefinite.
To avoid excessively strong dysregulations, the upper limit for the absolute value of the dysregulated correlation coefficient is set to:

\[
\min(0.9, 1.25 \times \max(\text{abs}(C[\text{upper.tri}(C)])))
\]

where \( C \) is the correlation matrix of the reference condition.

**Value**

It returns a list containing:
- data random samples generated from multivariate normal distributions with covariance matrices \( S_1 \) (reference condition) and \( S_2 \) (dysregulated condition);
- \( S_1, S_2 \) two covariance matrices;
- path the dysregulated path;
- strength the dysregulation strength for each edge in the path;
- \( \mu_1, \mu_2 \) two mean vectors;
- correction correction details.

**See Also**

`easyLookDys`, `easyLookShiny`, `plotCorGraph`, `plotGraphNELD3`

**Examples**

```r
if(require(gRbase) & require(graph)){
  ## Directed graph
  ## sub-graph Acute Myel... Leukemia
  graph<-gRbase::dag(~867:25+867:613+5295:867+5294:867+
    + 207:5295+207:5294+4193:287+3551:207+
    + 4792:3551+7157:4193+3265:6654+
    + 3845:6654+6654:2885+2885:25+2885:613)
  genes<-graph::nodes(graph)
  # covariance matrix of the reference condition
data<-t(chimera[genes,colnames(chimera)==1])
S<-cov(data)
S<-fitSgraph(graph,S)
  # select path to dysregulate
path<-list(c("613","867"),c("867","5295"),c("5295","207"),
    + c("207","4193"),c("4193","7157"))
  ## ..or select the path in an interactive plot
  # path<-getPathShiny(graph)
  # select parameters of the dysregulation
min<-c(2,8,2,0.1,0.5)
max<-c(2,10,2,4,0.5)
prob<-c(1,0,0,0.5,1)
}
```
```r
# activation, switch, switch, random, deactivation
dys <- cbind(min, max, prob)
rownames(dys) <- sapply(path, paste, collapse = "-")
dys

set.seed(123)
# main function
Result <- simPATHy(graph, path, S, min, max, prob)
class(Result)
names(Result)

# simulated data from two conditions
round(Result$dataset[c(1:3, 501:503), 1:5], 3)

# Summary
easyLookDys(Result)
# ..or interactive summary
easyLookShiny(resObj = Result, graph = graph)

# Visualization
plotCorGraph(S1 = Result$S1, S2 = Result$S2, graph = graph, path = path, colLim = c(-0.3, 0.3))
plotGraphNELD3(S1 = Result$S1, S2 = Result$S2, graph = graph, colLim = c(-0.3, 0.3))
rm(list = ls())

## Undirected graph
graph <- gRbase::ug(~a:b, ~a:c, ~c:d, ~b:d, ~b:c)
# when reference condition covariance matrix is not supplied simPATHy generate a random one
Result_ug <- simPATHy(graph)
easyLookDys(Result_ug)
plotGraphNELD3(S1 = Result_ug$S1, S2 = Result_ug$S2, graph = graph, colLim = c(-0.5, 0.5))
```

---

### SMLEdecomposable

**Local Maximum Likelihood Estimation**

#### Description

Compute a maximum likelihood estimate of a covariance matrix in a decomposable Gaussian graphical model.

#### Usage

`SMLEdecomposable(S, graph)`

#### Arguments

- `S` a covariance matrix.
- `graph` a decomposable graph represented as a graphNEL object.
Value

The MLE of a covariance matrix.

References

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