Package ‘BioNet’

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Description This package provides functions for the integrated analysis of protein-protein interaction networks and the detection of functional modules. Different datasets can be integrated into the network by assigning p-values of statistical tests to the nodes of the network. E.g. p-values obtained from the differential expression of the genes from an Affymetrix array are assigned to the nodes of the network. By fitting a beta-uniform mixture model and calculating scores from the p-values, overall scores of network regions can be calculated and an integer linear programming algorithm identifies the maximum scoring subnetwork.

License GPL (>= 2)

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BioNet-package

Routines for the functional analysis of biological networks

Description

This package provides functions for the integrated analysis of biological networks and the detection of functional modules. Different datasets can be integrated into the network by assigning p-values derived from statistical tests to the nodes of the network. E.g. p-values obtained from the differential expression of genes from an Affymetrix array are assigned to the nodes of a protein-protein interaction network. By fitting a beta-uniform mixture model and calculating scores from the p-values, overall scores of network regions can be calculated and an integer linear programming algorithm identifies the maximum scoring subnetwork.

Details

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Author(s)

Marcus Dittrich, Daniela Beisser
Maintainer: Marcus Dittrich <marcus.dittrich@biozentrum.uni-wuerzburg.de>

References


aggrPvals

Aggregate several p-values into one p-value

Description
The function aggregates several p-values into one p-value of p-values based on the order statistics of p-values. An overall p-value is given by the \(i\)th order statistic.

Usage
aggrPvals(pval.matrix, order, plot=TRUE)

Arguments
pval.matrix Numeric matrix of p-values, columns represent different sets of p-values
order Numeric constant, the order statistic that is used for the aggregation.
plot Boolean value whether to plot p-value distributions.

Value
Aggregated p-value of the given order.

Author(s)
Daniela Beisser

Examples
data(pvaluesExample)
aggrPvals(pval.matrix=pvaluesExample, order=2)

bumOptim

Fitting a beta-uniform mixture model to p-value distribution

Description
The function fits a beta-uniform mixture model to a given p-value distribution.

Usage
bumOptim(x, starts=1, labels=NULL)
**Arguments**

- `x`  Numerical vector of p-values, has to be named with the gene names or the gene names can be given in the labels parameter.
- `starts`  Number of start points for the optimization.
- `labels`  Gene names for the p-values.

**Value**

List of class fb with the following elements:

- `lambda`  Fitted parameter $\lambda$ for the beta-uniform mixture model.
- `a`  Fitted parameter $a$ for the beta-uniform mixture model.
- `negLL`  Negative log-likelihood.
- `pvalues`  P-value vector.

**Author(s)**

Marcus Dittrich and Daniela Beisser

**References**


**See Also**

`fitBumModel`, `plot.bum`, `hist.bum`

**Examples**

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bm <- bumOptim(x=pvals, starts=10)
bm
```
compareNetworks  

*Compare parameters of two networks*

**Description**

The function compares the following parameters of two networks: diameter, average degree, degree exponent, average path length and plots the cumulative degree distributions. The networks have to be connected components.

**Usage**

```r
compareNetworks(network1, network2, plot=TRUE)
```

**Arguments**

- `network1` : Network graphNEL or igraph format.
- `network2` : Second network in graphNEL or igraph format, or subnetwork drawn from first network.
- `plot` : Boolean value, whether to plot the cumulative degree distributions.

**Value**

A vector of network parameters is returned:

- `diam.network1` : Network diameter
- `diam.network2` : Diameter of the subnetwork
- `av.degree.network1` : Average degree of the network
- `av.degree.network2` : Average degree of the subnetwork
- `degree.exponent.network1` : Degree exponent of the network
- `degree.exponent.network2` : Degree exponent of the subnetwork
- `av.path.length.network1` : Average path length of the network
- `av.path.length.network2` : Average path length of the subnetwork

**Author(s)**

Daniela Beisser
Examples

library(DLBCL)
data(interactome)
subnet1 <- largestComp(subNetwork(nodes(interactome)[1:100], interactome))
subnet2 <- largestComp(subNetwork(nodes(interactome)[101:200], interactome))
compareNetworks(network1=subnet1, network2=subnet2)

consensusScores  

Calculation of a consensus score for a network

Description

The function calculates consensus scores for a network, given a list of replicate modules.

Usage

consensusScores(modules, network, ro=length(modules)/2)

Arguments

modules  
Calculated modules from pseudo-replicates of expression values in igraph or graphNEL format.

network  
Interaction network, which should be scores. In igraph or graphNEL format.

ro  
Threshold which is subtracted from the scores to obtain positive and negative value. The default value is half of the number of replicates.

Value

A result list is returned, consisting of:

N.scores  
Numerical vector node scores.

E.scores  
Numerical vector edge scores.

N.frequencies  
Numerical vector node frequencies from the replicate modules.

E.frequencies  
Numerical vector edge frequencies from the replicate modules.

Author(s)

Daniela Beisser
Examples

```
library(DLBCL)
data(interactome)
network <- interactome
# precomputed Heinz modules from pseudo-replicates
## Not run: lib <- file.path(.path.package("BioNet"), "extdata")
modules <- readHeinzGraph(node.file=file.path(datadir, "ALL_n_resample.txt.0.hnz"), network=network)
cons.scores <- consensusScores(modules, network)
## End(Not run)
```

---

fbum  
Compute the density of the bum distribution

Description

Function to compute the density of the beta-uniform mixture model.

Usage

```
fbum(x, lambda, a)
```

Arguments

- `x`: A numeric value.
- `lambda`: Parameter lambda, mixture parameter, proportion of uniform component
- `a`: Parameter a, shape parameter of beta component

Value

Value of the density of the bum distribution for `x`.

Author(s)

Marcus Dittrich

References


See Also

`bumOptim`, `fitBumModel`
Examples

```r
y <- fbum(x=0.5, lambda=0.1, a=0.1)
y
```

### Description

The function calculates the log likelihood of the BUM model.

### Usage

```r
fbumLL(parms, x)
```

### Arguments

- `parms` Vector of parameters; lambda and a.
- `x` Numerical vector of p-values.

### Value

Log likelihood.

### Author(s)

Marcus Dittrich

### Examples

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bum.mle <- fitBumModel(pvals, plot=FALSE)
fbumLL(parms=c(bum.mle$lambda, bum.mle$a), x=pvals)
```
fdrThreshold \hspace{1em} \textit{Calculate p-value threshold for given FDR}

\textbf{Description}

The function calculates the p-value threshold $\tau$ for a given false discovery rate. $\tau$ is used for the scoring function.

\textbf{Usage}

\begin{verbatim}
fdrThreshold(fdr, fb)
\end{verbatim}

\textbf{Arguments}

- \textbf{fdr} \hspace{1em} False discovery rate.
- \textbf{fb} \hspace{1em} Model from the beta-uniform mixture fitting.

\textbf{Value}

P-value threshold $\tau$.

\textbf{Author(s)}

Marcus Dittrich

\textbf{References}


\textbf{See Also}

\texttt{fbum, fitBumModel}

\textbf{Examples}

\begin{verbatim}
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bum.mle <- fitBumModel(pvals, plot=FALSE)
tau <- fdrThreshold(fdr=0.001, fb=bum.mle)
tau
\end{verbatim}
**fitBumModel**

*Fit beta-uniform mixture model to a p-value distribution*

**Description**

The function fits a beta-uniform mixture model to a given p-value distribution. The BUM method was introduced by Stan Pounds and Steve Morris to model the p-value distribution as a signal-noise decomposition. The signal component is assumed to be B(a,1)-distributed, whereas the noise component is uniform-distributed under the null hypothesis.

**Usage**

```r
fitBumModel(x, plot = TRUE, starts=10)
```

**Arguments**

- `x`: Numeric vector of p-values.
- `plot`: Boolean value, whether to plot a histogram and qqplot of the p-values with the fitted model.
- `starts`: Numeric value giving the number of starts for the optimization.

**Value**

Maximum likelihood estimator object for the fitted bum model. List of class fb with the following elements:

- `lambda`: Fitted parameter \( \lambda \) for the beta-uniform mixture model.
- `a`: Fitted parameter \( a \) for the beta-uniform mixture model.
- `negLL`: Negative log-likelihood.
- `pvalues`: P-value vector.

**Author(s)**

Daniela Beisser

**References**


**Examples**

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bum.mle <- fitBumModel(pvals, plot=TRUE)
bum.mle
```
getCompScores  
*Partition scores for subgraphs of the network*

Description
The function partitions the scores into scores for each subgraph of the network.

Usage
```
getCompScores(network, score)
```

Arguments
- `network`: A network in `graphNEL` or `igraph` format.
- `score`: Vector of scores.

Value
A data frame with the components of the network and the score for each PPI identifier.

Author(s)
Marcus Dittrich

Examples
```
library(DLBCL)
data(interactome)
data(dataLym)

# create random subgraph with 100 nodes and their direct neighbors
nodes <- nodes(interactome)[sample(length(nodes(interactome)), 100)]
subnet <- subNetwork(nodeList=nodes, network=interactome, neighbors="first")
score <- dataLym$score001
names(score) <- dataLym$label
getCompScores(score=score, network=subnet)
```

getEdgeList  
*Get representation of graph as edgelist*

Description
A network in `graphNEL` or `igraph` format is converted to an edgelist.

Usage
```
getEdgeList(network)
```
Arguments

network Network in graphNEL or igraph format.

Value

A matrix whose columns represent the connected edges.

Author(s)

Marcus Dittrich

Examples

library(DLBCL)
data(interactome)
getEdgeList(interactome)[1:10,]

hist.bum  

Histogram of the p-value distribution with the fitted bum model

Description

The function plots a histogram of the p-values together with the fitted bum-model.

Usage

## S3 method for class 'bum'
hist(x, breaks=50, main="Histogram of p-values", xlab="P-values", ylab="Density", ...)

Arguments

x Maximum likelihood estimator object of the beta-uniform mixture fit.
breaks Breaks for the histogram.
main An overall title for the plot.
xlab A title for the x axis.
ylab A title for the y axis.
... Other graphic parameters for the plot.

Author(s)

Daniela Beisser

See Also

fitBumModel, hist.bum, bumOptim
Examples

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
mle <- fitBumModel(pvals, plot=FALSE)
hist(mle)
```

---

**largestComp**

*Extract largest component of network*

### Description

The function extracts the largest component of a network.

### Usage

```r
largestComp(network)
```

### Arguments

- **network**  
  A graph in `graphNEL` or `igraph` format.

### Value

A new graph object that represents the largest component of the given network.

### Author(s)

Marcus Dittrich

### Examples

```r
library(DLBCL)
data(interactome)
interactome
largestComp(interactome)
```
**largestScoreComp**

**Component with largest score**

**Description**

The function extracts the component of the network with the largest score. All nodes have to exceed the given level for the score.

**Usage**

```r
largestScoreComp(network, score, level=0)
```

**Arguments**

- `network`: Network in `graphNEL` or `igraph` format.
- `score`: Vector of scores for the network.
- `level`: Cut-off level for the score for the component.

**Value**

Subgraph of the network with a score larger than the given level.

**Author(s)**

Marcus Dittrich

**Examples**

```r
library(DLBCL)
data(interactome)
data(dataLym)
network <- rmSelfLoops(interactome)
score <- dataLym$score001
names(score) <- dataLym$label
lComp <- largestScoreComp(network=network, score=score, level=1)
## Not run: plotModule(lComp)
```
loadNetwork.sif

Load network from Cytoscape sif file

Description

The function loads a network from a Cytoscape sif file. Edge attributes are provided in the ea.file or vector of ea.files. The node attributes are provided the same way. For other formats see read.graph in the igraph package.

Usage

loadNetwork.sif(sif.file, na.file, ea.file, format=c("graphNEL", "igraph"), directed=FALSE)

Arguments

- **sif.file**: Cytoscape sif file, containing the network.
- **na.file**: File or vector of file with Cytoscape node attributes.
- **ea.file**: File or vector of file with Cytoscape edge attributes.
- **format**: Format of output graph, either graphNEL or igraph.
- **directed**: Boolean value for directed or undirected graph.

Value

Graph with loaded attributes.

Author(s)

Daniela Beisser

Examples

```r
## Not run: lib <- file.path(.path.package("BioNet"), "extdata")
# load interaction file, node attribute file with a node weight of 2 for each node and the edge attribute file with a edge weight of 1 for each edge
network <- loadNetwork.sif(sif.file=file.path(lib,"cytoscape.sif"), na.file=file.path(lib,"n.weight.NA"), ea.file=file.path(lib,"e.weight.EA"), format="graphNEL", directed=FALSE);
nodeData(network);
edgeData(network);
## End(Not run)
```
loadNetwork.tab  Load network from tabular format

Description
The function loads a network from a tabular format.

Usage
loadNetwork.tab(file, header=TRUE, directed=FALSE, format=c("graphNEL", "igraph"))

Arguments
- file: File with network to load.
- header: Boolean value whether to include header or not.
- directed: Boolean value whether the network is to be directed or not.
- format: Output format of the network, either graphNEL or igraph

Author(s)
Marcus Dittrich

See Also
- loadNetwork.sif

makeNetwork  Create graph from source and target vectors

Description
Function to create a graph in graphNEL or igraph format from a source and a target vector.

Usage
makeNetwork(source, target, edgemode="undirected", format=c("graphNEL", "igraph"))

Arguments
- source: Vector of source nodes.
- target: Vector of corresponding target nodes.
- edgemode: For an "undirected" or "directed" network.
- format: Graph format, either graphNEL or igraph.
The function selects for each gene the probeset with the highest variance and gets the PPI ID for each gene. The PPI identifier is: gene symbol(Entrez ID). Affymetrix identifiers are mapped to the ENTREZ ID.

Usage

```r
code
mapByVar(exprSet, network=NULL, attr="geneID", ignoreAFFX=TRUE)
```

Arguments

- `exprSet`: Affymetrix ExpressionSet.
- `network`: Network that is used to map the Affymetrix identifiers.
- `attr`: The attribute of the network that is used to map the Affymetrix IDs. The IDs are mapped to the unique Entrez gene IDs, which are by default stored in the "geneID" attribute of the network.
- `ignoreAFFX`: Boolean value, whether to ignore or leave AFFX control genes.

Value

Expression matrix with one gene (PPI ID) per probeset.

Author(s)

Daniela Beisser
Examples

```r
## Not run: library(ALL);
data(ALL);
mapped.e.set <- mapByVar(ALL);
mapped.e.set[1:10,];
## End(Not run)
```

---

**permutateNodes**  
*Permute node labels*

**Description**

Function to permutate node labels of a given network.

**Usage**

```r
permutateNodes(network)
```

**Arguments**

- `network`  
  Network in `graphNEL` or `igraph` format.

**Value**

Network with permutated labels.

**Author(s)**

Marcus Dittrich

**Examples**

```r
library(DLBCL)
data(interactome)
# remove self-loops before permutating the labels
interactome <- rmSelfLoops(interactome)
perm.net <- permutateNodes(interactome)
perm.net
```
\textbf{piUpper} \hspace{1cm} \textit{Upper bound pi for the fraction of noise}

\textbf{Description}

The function calculates the upper bound pi for the fraction of noise.

\textbf{Usage}

\texttt{piUpper(fb)}

\textbf{Arguments}

\begin{itemize}
  \item \texttt{fb} Fitted bum model, list with parameters a and lambda.
\end{itemize}

\textbf{Value}

Numerical value for the upper bound pi.

\textbf{Author(s)}

Marcus Dittrich

\textbf{See Also}

\texttt{bumOptim}, \texttt{fitBumModel}

\textbf{Examples}

\begin{verbatim}
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bum <- bumOptim(pvals, starts=10)
piUpper(fb=bum)
\end{verbatim}

\textbf{plot.bum} \hspace{1cm} \textit{Quantile-quantile plot for the beta-uniform mixture model}

\textbf{Description}

The function plots the theoretical quantiles of the fitted bum model against the quantiles of the observed p-value distribution.

\textbf{Usage}

\begin{verbatim}
## S3 method for class 'bum'
plot(x, main="QQ-Plot", xlab="Estimated p-value", ylab="Observed p-value", ...)
\end{verbatim}
plot3dModule

Arguments

- `x` Maximum likelihood estimation object of the fitted bum model.
- `main` An overall title for the plot.
- `xlab` A title for the x axis.
- `ylab` A title for the y axis.
- `...` Other graphic parameters for the plot.

Author(s)

Daniela Beisser

See Also

`fitBumModel, plot.bum, bumOptim`

Examples

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
mle <- fitBumModel(pvals, plot=FALSE)
plot(mle)
```

Description

The function plots a network from `graphNEL` or `igraph` format in 3D using a modified function from the package igraph and requires the package rgl which uses openGL. The 3D plot can be zoomed, rotated, shifted on the canvas. This function is just used to visualize the modules. For further plotting options use the rglplot function of the igraph package. If a score attribute is provided in the graph this will be used for the coloring of the nodes. Otherwise a vector of values can be given by the `diff.or.score` argument. The vector has to contain positive and negative values, either scores or values for differential expression (fold changes). Labels for the nodes can be provided by the `labels` argument, otherwise it will be automatically looked for a `geneSymbol` attribute of the nodes.

Usage

```r
plot3dModule(network, labels=NULL, windowSize = c(100,100,1500,1000), diff.or.scores=NULL, red=c("negative", "positive"), ...)
```
Arguments

<table>
<thead>
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<th>Description</th>
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<tr>
<td>network</td>
<td>Network in graphNEL or igraph format.</td>
</tr>
<tr>
<td>labels</td>
<td>Labels for the nodes of the network. Otherwise it will be automatically looked for a geneSymbol attribute of the nodes.</td>
</tr>
<tr>
<td>windowSize</td>
<td>Numerical vector of size four to set the size of the rgl device.</td>
</tr>
<tr>
<td>diff.or.scores</td>
<td>Named numerical vector of differential expression (fold changes) or scores of the nodes in the network. These will be used for node coloring. Otherwise a score attribute of the nodes will be automatically used.</td>
</tr>
<tr>
<td>red</td>
<td>Either &quot;negative&quot; or &quot;positive&quot;, to specify which values are to be colored red in the plot.</td>
</tr>
<tr>
<td>...</td>
<td>Other graphic parameters for the plot.</td>
</tr>
</tbody>
</table>

Author(s)

Daniela Beisser

See Also

save3dModule, plotModule

Examples

```r
library(DLBCL)
data(interactome)
data(dataLym)
interactome <- subNetwork(dataLym$label, interactome)
interactome <- rmSelfLoops(interactome)
fchange <- dataLym$diff
names(fchange) <- dataLym$label
subnet <- largestComp(subNetwork(nodes(interactome)[1:100], interactome))
diff <- fchange[nodes(subnet)]

## Not run: library(rgl);
plot3dModule(network=subnet, diff.or.score=diff)
## End(Not run)
```

plotLLSurface      Log likelihood surface plot

Description

The function plots the log likelihood surface for all a and lambda parameter of the beta-uniform mixture model.

Usage

plotLLSurface(x, opt=NULL, main="Log-Likelihood Surface", color.palette = heat.colors, nlevels = 32)
**plotModule**

**Arguments**

- **x**  
  Numeric vector of p-values.

- **opt**  
  List of optimal parameters for a and lambda from the beta-uniform mixture model.

- **main**  
  The overall title of the plot.

- **color.palette**  
  Color scheme of the image plot.

- **nlevels**  
  Number of color levels.

**Author(s)**

Marcus Dittrich

**Examples**

```r
library(DLBCL)
data(dataLym)
pvals <- dataLym$t.pval
names(pvals) <- dataLym$label
mle <- fitBumModel(pvals, plot=FALSE)
plotLLSurface(x=pvals, opt=mle)
```

**Description**

The function plots a network from `graphNEL` or `igraph` format, adapted from an igraph plotting function. It is just used to visualize the modules. For further plotting options use the `plot.igraph` function of the igraph package. The shapes of the nodes can be changed according to the scores argument, then negative scores appear squared. The color of the nodes can be changed according to the `diff.expr` argument. Negative values lead to green nodes, positive values are colored in red. If the vectors are not provided, it will be automatically looked for nodes attributes with the name `score` and `diff.expr`.

**Usage**

```r
plotModule(network, layout=layout.fruchterman.reingold, labels=NULL, diff.expr=NULL, scores=NULL, main=NULL, vertex.size=NULL, ...)
```

**Arguments**

- **network**  
  Network in `graphNEL` or `igraph` format.

- **layout**  
  Layout algorithm, e.g. `layout.fruchterman.reingold` or `layout.kamada.kawai`.

- **labels**  
  Labels for the nodes of the network.
diff.expr  Named numerical vector of differential expression (fold changes) of the nodes in the network. These will be used for coloring of the nodes. It will be automatically looked for nodes attribute with the name diff.expr, if the argument is null.

scores    Named numerical vector of scores of the nodes in the network. These will be used for the shape of the nodes. It will be automatically looked for nodes attribute with the name score, if the argument is null.

main      Main title of the plot.

vertex.size Numerical value or vector for the size of the vertices.

...       Other graphic parameters for the plot.

Author(s)

Marcus Dittrich and Daniela Beisser

See Also

plot3dModule

Examples

```r
library(DLBCL)
data(dataLym)
data(interactome)
interactome <- subNetwork(dataLym$label, interactome)
interactome <- rmSelfLoops(interactome)
fchange <- dataLym$diff
names(fchange) <- dataLym$label
# create random subnetwork
subnet <- largestComp(subNetwork(nodes(interactome)[1:100], interactome))
fchange <- fchange[nodes(subnet)]

# color random subnetwork by the fold change
## Not run: plotModule(network=subnet, diff.expr=fchange)
```

### print.bum

*Print information about bum model*

Description

The function prints information about the bum model.

Usage

```r
## S3 method for class 'bum'
print(x, ...)
```
pvaluesExample

Arguments

- **x**  
  Maximum likelihood estimator object of the beta-uniform mixture fit.

- **...**  
  Other graphic parameters for print.

Author(s)

Marcus Dittrich

See Also

fitBumModel, summary.bum

Examples

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
mle <- fitBumModel(pvals, plot=FALSE)
print(mle)
```

Description

Data example consisting of a matrix of p-values. Each gene has two corresponding p-values. These p-values can be aggregated into a p-value of p-values by the method `aggrPvals`.

Usage

```r
data(pvaluesExample)
```

Examples

```r
data(pvaluesExample)
pvaluesExample[1:10,]
```
readHeinzGraph  

Convert HEINZ output to graph

Description

Function to convert the HEINZ output to a graph object, or if the output is in matrix form, it will create a list of graphs. The function needs the node and the original network, from which the module is calculated.

Usage

readHeinzGraph(node.file, network, format=c("graphNEL", "igraph"))

Arguments

node.file  Heinz node output file.
network  Original network from which Heinz input was created.
format  Graph format of output, either igraph or graphNEL.

Value

Graph object.

Author(s)

Daniela Beisser

Examples

library(DLBCL)
data(interactome)
# precomputed Heinz output files
## Not run: lib <- file.path(path.package("BioNet"), "extdata")
module <- readHeinzGraph(node.file=file.path(lib, "lymphoma_nodes_001.txt.0.hnz"), network=interactome, format="graphNEL"; plotModule(module);
## End(Not run)
Description

Converts the HEINZ output to a tree in graph format. If the output is in matrix form, it will create a list of graphs. The function needs the node and edge file and the original network from which the module is calculated.

Usage

readHeinzTree(node.file, edge.file, network, format=c("graphNEL", "igraph"))

Arguments

node.file  Heinz node output file.
edge.file  Heinz edge output file.
network    Original network from which Heinz input was created.
format     Output format of the graph, either igraph or graphNEL.

Value

A graph object.

Author(s)

Daniela Beisser

Examples

library(DLBCL)
data(interactome)
# precomputed Heinz output files
## Not run: lib <- file.path(.path.package("BioNet"), "extdata")
module <- readHeinzTree(node.file=file.path(lib, "lymphoma_nodes_001.txt.0.hnz"), edge.file=file.path(lib, "lymphoma_nodes_001.txt.0.hnz"), network=interactome, format="graphNEL")
plotModule(module);

## End(Not run)
resamplingPvalues  

Resampling of microarray expression values and test for differential expression.

Description

The function uses a 50% jackknife resampling to calculate a pseudo-replicate of the expression matrix. The resampled expression values are used thereupon to calculate p-values for the differential expression between the given groups. Only two-group comparisons are allowed for the performed t-test.

Usage

resamplingPvalues(exprMat, groups, alternative = c("two.sided", "less", "greater"), resampleMat=FALSE)

Arguments

exprMat  
Matrix with microarray expression values.

groups  
Factors for two groups that are tested for differential expression.

alternative  
Testing alternatives for the t-test: "two.sided", "less" or "greater".

resampleMat  
Boolean value, whether to retrieve the matrix of jacknife resamples or not.

Value

A result list is returned, consisting of:

p.values  
Numerical vector of p-values.

resampleMat  
Matrix of resampled expression values.

Author(s)

Daniela Beisser

Examples

library(ALL)
data(ALL)
mat <- exprs(ALL)
groups <- factor(c(rep("A", 64), rep("B", 64)))
results <- resamplingPvalues(mat, groups, alternative="greater")
**rmSelfLoops**

*Remove self-loops in a graph*

**Description**

The function removes self-loops, edges that start and end in the same node, from the network.

**Usage**

```r
rmSelfLoops(network)
```

**Arguments**

- `network` A graph object, either in `graphNEL` or `igraph` format.

**Value**

The graph with the removed edges.

**Author(s)**

Marcus Dittrich

**Examples**

```r
graph <- makeNetwork(c("a","b","c","d","e","a"), c("b","c","d","e","e","e"))
graph2 <- rmSelfLoops(graph)
edges(graph)
edges(graph2)
```

---

**runFastHeinz**

*Calculate heuristically maximum scoring subnetwork*

**Description**

The function uses an heuristic approach to calculate the maximum scoring subnetwork. Based on the given network and scores the positive nodes are in the first step aggregated to meta-nodes between which minimum spanning trees are calculated. In regard to this, shortest paths yield the approximated maximum scoring subnetwork. This function can be used if a CPLEX license is not available to calculate the optimal solution.

**Usage**

```r
runFastHeinz(network, scores)
```
Arguments

network A graph in igraph or graphNEL format.
scores A named vector, containing the scores for the nodes of the network. All nodes need to be scored in order to run the algorithm.

Value

A subnetwork in the input network format.

Author(s)

Daniela Beisser

See Also

writeHeinzEdges, writeHeinzNodes, readHeinzTree, readHeinzGraph, runHeinz

Examples

library(DLBCL)
# load p-values
data(dataLym)
# load graph
data(interactome)
# get induced subnetwork for all genes contained on the chip
interactome <- subNetwork(dataLym$label, interactome)
p.values <- dataLym$t.pval
names(p.values) <- dataLym$label
bum <- fitBumModel(p.values, plot=TRUE)
scores <- scoreNodes(network=interactome, fb=bum, fdr=0.0001)
module <- runFastHeinz(network=interactome, scores=scores)
## Not run: plotModule(module)

runHeinz

Start HEINZ

Description

The function starts HEINZ from command line. The HEINZ folder has to include the heinz.py python script and the dhea file. CPLEX has to be installed and accessible from the computer R runs on.

Usage

runHeinz(heinz.folder="", heinz.e.file, heinz.n.file, N=TRUE, E=FALSE, diff=-1, n=1)
Arguments

heinz.folder  The folder which contains the heinz.py python script and the dhea file.
heinz.e.file  The HEINZ edge input file. See writeHeinzEdges
heinz.n.file  The HEINZ node input file. See writeHeinzNodes
N  Boolean value, whether to run HEINZ on nodes.
E  Boolean value, whether to run HEINZ on edges. HEINZ can run on both with N and E set to TRUE.
diff  Difference of suboptimal solutions to optimal solution in hamming distance in percent. Parameter is set to -1 for optimal solution.
n  Number of optimal and suboptimal solutions, the standard n=1 delivers only the optimal solution.

Details

This function starts the integer linear programming algorithm to calculate the optimal scoring sub-network. The algorithm might be started in the command line when the CPLEX is installed on another machine. To start it from command line use: heinz.py -e edge.file.txt -n node.file.txt -E False/True -N False/True. The results can be loaded with readHeinzTree, readHeinzGraph as a graph object.

Author(s)

Daniela Beisser

References


See Also

writeHeinzEdges, writeHeinzNodes, readHeinzTree, readHeinzGraph

save3dModule  Save a 3D plot of the network

Description

The function saves a 3D plot of a network to file, therefore it requires the plot to be open. A screenshot of the 3D plot can be saved in "pdf" format. Background of the device is changed to white for plotting. The screenshot can take several seconds for large plots.

Usage

save3dModule(file)
Arguments

- **file**: File to save to.

Author(s)

Daniela Beisser

See Also

`plot3dModule`, `plotModule`

Examples

```r
library(DLBCL)
data(dataLym)
data(interactome)
interactome <- subNetwork(dataLym$label, interactome)
fchange <- dataLym$diff
names(fchange) <- dataLym$label
subnet <- largestComp(subNetwork(nodes(interactome)[1:100], interactome))
diff <- fchange[nodes(subnet)]

## Not run: library(rgl);
plot3dModule(network=subnet, diff.or.score=diff);
save3dModule(file="test")
## End(Not run)
```

---

**saveNetwork**

Save undirected network in various formats

Description

The function saves a graph in a Cytoscape readable format: either in XGMML format, or as two tables, one for the nodes with attributes and one for the edges with attributes, or as .sif file. Or other standard formats like tab separated, .tgf, .net

Usage

```r
saveNetwork(network, name="network", file, type=c("table", "XGMML", "sif", "tab", "tgf", "net"))
```

Arguments

- **network**: Network to save.
- **name**: Name of the network, only needed for the XGMML format.
- **file**: File to save to.
- **type**: Type in which graph shall be saved.
Details

The format types are "XGMML", "table", "sif", "tab", "tgf" and "net". XGMML (eXtensible Graph Markup and Modeling Language) is an XML format based on GML which is used for graph description. Edges, nodes and their affiliated attributes are all saved in one file. In the table format two tables are created, one for the nodes with attributes and one for the edges with attributes. The sif format creates a .sif file for the network and an node attribute (.NA) or edge attribute (.EA) for each attribute. The name of the attribute is the filename. Tab writes only the edges of the network in a tabular format. Tgf save the network to simple .tgf format. The net format writes a Pajek readable file of the network and the ET type saves the edge tags to file.

Author(s)

Daniela Beisser and Marcus Dittrich

Examples

library(DLBCL)
# create small network
library(igraph)
data(interactome)
interactome <- igraph.from.graphNEL(interactome)
small.net <- subNetwork(V(interactome)[1:16]$name, interactome)
E(small.net)$e.weight <- rep(1,length(E(small.net)))
V(small.net)$n.weight <- rep(2,length(V(small.net)))
summary(small.net)
## Not run: saveNetwork(small.net, file="example_network", name="small.net", type="XGMML")

scanFDR

Dataframe of scores over a given range of FDRs

Description

The function generates a dataframe for a given range of FDRs.

Usage

scanFDR(fb, fdr, labels=names(fb$pvalues))

Arguments

fb Fitted bum model.
fdr Vector of FDRs.
labels Data frame labels.

Value

Dataframe of scores for given p-values and a range of FDRs.
scoreFunction

Author(s)
Marcus Dittrich

See Also
bumOptim, fitBumModel

Examples

data(pvaluesExample)
pvals <- pvaluesExample[,1]
bm <- bumOptim(pvals, starts=10)
scores <- scanFDR(fb=bm, fdr=c(0.1, 0.001, 0.0001))
scores[1:10,]

Description
The function calculates a score for each gene with a given FDR from the fitted beta-uniform mixture model.

Usage
scoreFunction(fb, fdr=0.01)

Arguments
fb Model from the beta-uniform mixture fitting.
fdr Numeric constant, from the false discovery rate a p-value threshold is calculated. P-values below this threshold are considered to be significant and will score positively, p-values above the threshold are supposed to arise from the null model. The FDR can be used to control the size of the maximum scoring subnetwork, by zooming in and out in the same region.

Value
Score vector for the given p-values.

Author(s)
Marcus Dittrich and Daniela Beisser

References
scoreNodes

Examples

data(pvaluesExample)
pvals <- pvaluesExample[,1]
bum.mle <- fitBumModel(pvals, plot=FALSE)
scores <- scoreFunction(fdr=0.1, fb=bum.mle)
scores

scoreNodes  Score the nodes of a network

Description

The function derives scores from the p-values of the nodes of a network.

Usage

scoreNodes(network, fb, fdr=0.05)

Arguments

network  A network in graphNEL or igraph format.
fb  Fitted bum model.
fdr  False discovery rate.

Value

Ordered score vector for the nodes of the network.

Author(s)

Marcus Dittrich

See Also

bumOptim, fitBumModel

Examples

library(DLBCL)
# load p-values
data(dataLym)
# load graph
data(interactome)
# get induced subnetwork for all genes contained on the chip
chipGraph <- subNetwork(dataLym$label, interactome)
p.values <- dataLym$t.pval
names(p.values) <- dataLym$label
bum <- fitBumModel(p.values, plot=TRUE)
scoreNodes(network=chipGraph, fb=bum, fdr=0.001)
scoreOffset  

*Change score offset for 2 FDRs*

**Description**

Function to change score offset from FDR1 to FDR2.

**Usage**

```r
scoreOffset(fb, fdr1, fdr2)
```

**Arguments**

- `fb`: Model from the beta-uniform mixture fitting.
- `fdr1`: First false discovery rate.
- `fdr2`: Second false discovery rate.

**Value**

Offset for the score of the second FDR.

**Author(s)**

Marcus Dittrich

**See Also**

`bumOptim`, `fitBumModel`

**Examples**

```r
data(pvaluesExample)
pvals <- pvaluesExample[,1]
bm <- bumOptim(pvals, starts=10)
scoreOffset(bm, fdr1=0.001, fdr2=0.000001)
```
**sortedEdgeList**

*Get a sorted edgelist*

**Description**

Function to get a sorted edgelist where the source protein is alphabetically smaller than the target protein from an undirected network.

**Usage**

```r
sortedEdgeList(network)
```

**Arguments**

- `network`: Undirected network in *igraph* or *graphNEL* format.

**Value**

Vector of sorted edges, where the source protein is alphabetically smaller than the target protein.

**Author(s)**

Daniela Beisser

**Examples**

```r
library(DLBCL)
data(interactome)
E.list <- sortedEdgeList(interactome)
```

---

**subNetwork**

*Create a subGraph*

**Description**

The function creates a subgraph with the nodes given in the `nodeList` or for these nodes including their direct neighbors.

**Usage**

```r
subNetwork(nodeList, network, neighbors=c("none", "first"))
```

**Arguments**

- `nodeList`: Character vector of nodes, contained in the subgraph.
- `network`: Graph that is used for subgraph extraction.
- `neighbors`: Neighborhood, that is chosen for the subgraph extraction. "none" are only the selected nodes, "first" includes the direct neighbors of the selected nodes.
summary.bum

Print summary of informations about bum model

Description

The function summarizes information about the bum model.

Usage

## S3 method for class 'bum'
summary(object, ...)

Arguments

object Maximum likelihood estimator object of the beta-uniform mixture fit.
...
Other graphic parameters for summary.

Author(s)

Daniela Beisser
See Also

fitBumModel, print.bum

Examples

data(pvaluesExample)
pvals <- pvaluesExample[,1]
mle <- fitBumModel(pvals, plot=FALSE)
summary(mle)

writeHeinz

Write input files for HEINZ

Description

Function to write the input files with the node and edge scores for HEINZ. These files are used to calculate the maximum scoring subnetwork of the graph. The node scores are matched by their names to the nodes of the network, therefore if nodes.scores are provided as a vector or matrix, the vector has to be named, respectively the matrix has to be provided with rownames. If the network contains more nodes than the score vector, the nodes without a score are scored with the average over all nodes. If the nodes should not be scored and used for the calculation of the maximum scoring subnetwork, draw a subnetwork (subNetwork) first and use this for the argument network. The edge scores can be provided as a vector or matrix as the edge.scores argument. If no scores are provided in the arguments, but the use.node.scores or use.edge.scores argument is set to TRUE, it will be automatically looked for the "score" attribute of the nodes and edges of the network.

Usage

writeHeinz(network, file, node.scores=0, edge.scores=0, use.node.score=FALSE, use.edge.score=FALSE)

Arguments

network  Network from which to calculate the maximum scoring subnetwork.
file     File to write to.
node.scores  Numeric vector or matrix of scores for the nodes of the network. Names of the vector or rownames of the matrix have to correspond to the PPI identifiers of the network. The scores can also be used from the node attribute "score", given one score for each node.
esday.scores  Numeric vector of scores for the edges of the network. Edge scores have to be given in the order of the edges in the network. It is better to append the edge scores as the edge attribute "score" to the network: V(network)$score and set use.scores to TRUE.
use.node.score Boolean value, whether to use the node attribute "score" in the network as node scores.
use.edge.score Boolean value, whether to use the edge attribute "score" in the network as edge scores.
writeHeinzEdges

Author(s)
Daniela Beisser

See Also
writeHeinzNodes and writeHeinzEdges

Examples
library(DLBCL)
# use Lymphoma data and graph to find module
data(interactome)
data(dataLym)
# get induced subnetwork for all genes contained on the chip
chipGraph <- subNetwork(dataLym$label, interactome)
# get the score for the subnetwork
score <- dataLym$score001
# names(score) <- dataLym$label
## Not run: writeHeinz(network=chipGraph, file="lymphoma_001", node.scores=score, edge.scores=0)

writeHeinzEdges file file Write edge input file for HEINZ

Description
Function to write an input file for HEINZ with edge scores. If no edge scores are used, they are set to 0. In order to run HEINZ, a node input and edge input file are needed.

Usage
writeHeinzEdges(network, file, edge.scores=0, use.score=FALSE)

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>network</td>
<td>Network from which to calculate the maximum scoring subnetwork.</td>
</tr>
<tr>
<td>file</td>
<td>File to write to.</td>
</tr>
<tr>
<td>edge.scores</td>
<td>Numeric vector of scores for the edges of the network. Edge scores have to be given in the order of the edges in the network. It is better to append the edge scores as the edge attribute &quot;score&quot; to the network: ( V(network)$score ) and set use.score to TRUE.</td>
</tr>
<tr>
<td>use.score</td>
<td>Boolean value, whether to use the edge attribute &quot;score&quot; in the network as edge scores.</td>
</tr>
</tbody>
</table>

Author(s)
Daniela Beisser
writeHeinzNodes

See Also

writeHeinzNodes and writeHeinz

Examples

library(DLBCL)
# use Lymphoma data and graph to find module
data(interactome)
data(dataLym)
# get induced subnetwork for all genes contained on the chip
chipGraph <- subNetwork(dataLym$label, interactome)
# remove self loops
graph <- rmSelfLoops(chipGraph)
## Not run: writeHeinzEdges(network=graph, file="lymphoma_edges_001", use.score=FALSE)
score <- dataLym$score001
names(score) <- dataLym$label
## Not run: writeHeinzNodes(network=graph, file="lymphoma_nodes_001", node.scores=score)

# write another edge file with edge scores
library(igraph)
data(interactome)
interactome <- igraph.from.graphNEL(interactome)
small.net <- subNetwork(V(interactome)[1:16]$name, interactome)
scores <- c(1:length(E(small.net)))
E(small.net)$score <- scores
## Not run: writeHeinzEdges(network=small.net, file="test_edges", use.score=TRUE)

writeHeinzNodes

Write node input file for HEINZ

Description

Function to write an input file with the node scores for HEINZ. This file is used together with the edge input file to calculate the maximum scoring subnetwork of the graph. The scores are matched by their names to the nodes of the network, therefore if nodes.scores are provided as a vector or matrix, the vector has to be named, respectively the matrix has to be provided with rownames. If the network contains more nodes than the score vector, the nodes without a score are scored with the average over all nodes. If the nodes should not be scored and used for the calculation of the maximum scoring subnetwork, draw a subnetwork subNetwork first and use this for the argument network.

Usage

writeHeinzNodes(network, file, node.scores=0, use.score=FALSE)
writeHeinzNodes

Arguments

- **network**: Network from which to calculate the maximum scoring subnetwork.
- **file**: File to write to.
- **node.scores**: Numeric vector or matrix of scores for the nodes of the network. Names of the vector or rownames of the matrix have to correspond to the PPI identifiers of the network. The scores can also be used from the node attribute "score", given one score for each node.
- **use.score**: Boolean value, whether to use the node attribute "score" in the network as node scores.

Details

Use `scoreNodes` or `scoreFunction` to derive scores from a vector of p-values.

Author(s)

Daniela Beisser

See Also

`writeHeinzEdges` and `writeHeinz`

Examples

```r
# create small network
library(DLBCL)
data(interactome)
small.net <- subNetwork(nodes(interactome)[0:15], interactome)
scores <- c(1:length(nodes(small.net)))
names(scores) <- nodes(small.net)
## Not run: writeHeinzNodes(network=small.net, file="test_nodes", node.scores=scores)

# use Lymphoma data and graph to find module
library(DLBCL)
data(dataLym)
# get induced subnetwork for all genes contained on the chip
chipGraph <- subNetwork(dataLym$label, interactome)
## Not run: writeHeinzEdges(network=chipGraph, file="lymphoma_edges_001", use.score=FALSE)
score <- dataLym.score001
names(score) <- dataLym$label
## Not run: writeHeinzNodes(network=chipGraph, file="lymphoma_nodes_001", node.scores=score)
```
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