Package 'ROntoTools'

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Type Package

Title R Onto-Tools suite

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Description Suite of tools for functional analysis

License GPL (>= 3)

Depends methods, graph, boot, KEGGREST, KEGGgraph, Rgraphviz

Suggests RUnit, BiocGenerics

Collate 'pathwayExpress.R' 'utils.R' 'graphWeights.R' 'keggDataREST.R'
'AllClasses.R' 'AllGenerics.R' 'nodeWeights-methods.R'
'pePathway-utils.R' 'Summary-methods.R' 'plot-methods.R' 'renderInfo-methods.R'

biocViews Network, Microarray, GraphAndNetwork

R topics documented:

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alpha1MR *Compute alpha weights*

Description

Transform a vector of p-values into weights.

Usage

```
alpha1MR(pv, threshold = max(pv))
```

Arguments

pv   vector of p-values

threshold   the threshold value that was used to select DE genes

Details

Computes a set of weights from p-values using the formula `1-pv/threshold`.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[pe](#)

Examples

```
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))

head(alpha1MR(top$adj.P.Val))
```

---

alphaMLG *Compute alpha weights*

Description

Transform a vector of p-values into weights.

Usage

```
alphaMLG(pv, threshold = max(pv))
```

Arguments

pv	vector of p-values
threshold	the threshold value that was used to select DE genes

Details

Computes a set of weights from p-values using the formula `-log10(pv/threshold)`.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[pe](pe)

Examples

```
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))

head(alphaMLG(top$adj.P.Val))
```

---

compute.fisher *Combine independent p-values using the Fisher method*

Description

Combine independent p-values using the Fisher method

Usage

```
compute.fisher(p, eps = 1e-06)
```

Arguments

p	a vector of independent p-values
eps	the minimal p-value considered (all p-values smaller will be set to this value)

Author(s)

Calin Voichita and Sorin Draghici

References

Tarca AL., Draghici S., Khatri P., Hassan SS., Kim J., Kim CJ., Kusanovic JP., Romero R.: "A Signaling Pathway Impact Analysis for Microarray Experiments", 2008, Bioinformatics, 2009, 25(1):75-82.

See Also

[pe](#),[compute.normalInv](#)

Examples

```
p <- c(.1, .01)
compute.fisher(p)
```

---

compute.normalInv	*Combine independent p-values using the normal inversion method*

Description

Combine independent p-values using the normal inversion method

Usage

```
compute.normalInv(p, eps = 1e-06)
```

Arguments

p	a vector of independent p-values
eps	the minimal p-value considered (all p-values smaller will be set to this value)

Author(s)

Calin Voichita and Sorin Draghici

References

Tarca AL., Draghici S., Romero R.: "A Mmore Specific Method To Combine Perturbation and Over-representation Evidence in Pathway Analysis", PSB 2010 poster.

See Also

[pe](), [compute.fisher]()

Examples

```
p <- c(.1, .01)
compute.normalInv(p)
```

---

keggPathwayGraphs   *Download and parse KEGG pathway data*

Description

Download and parse KEGG pathway data

Usage

```
keggPathwayGraphs(organism = "hsa",
  targRelTypes = c("GErel", "PCrel", "PPrel"),
  relPercThresh = 0.9, nodeOnlyGraphs = FALSE,
  updateCache = FALSE, verbose = TRUE)
```

Arguments

organism	organism code as defined by KEGG
targRelTypes	target relation types
relPercThresh	percentage of the number of relation types over all possible realtions in the pathway
nodeOnlyGraphs	allow graphs with no edges
updateCache	re-download KEGG data
verbose	show progress of downloading and parsing

Value

A list of [graphNEL]() objects encoding the pathway information.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[keggPathwayNames]()

Examples

```
# The pathway cache provided as part of the pathway contains only the
# pathways that passed the default filtering. We recommend, re-downloading
# the pathways using the updateCache parameter
kpg <- keggPathwayGraphs("hsa")

# to update the pathway cache for human run:
# kpg <- keggPathwayGraphs("hsa", updateCache = TRUE)
# this is time consuming and depends on the available bandwith.

head(names(kpg))

kpg[["path:hsa04110"]]
head(nodes(kpg[["path:hsa04110"]]))
head(edges(kpg[["path:hsa04110"]]))
```

---

keggPathwayNames   *Obtain KEGG pathway titles*

Description

Obtain KEGG pathway titles

Usage

```
keggPathwayNames(organism = "hsa", updateCache = FALSE,
  verbose = TRUE)
```

Arguments

organism	organism code as defined by KEGG
updateCache	re-download KEGG data
verbose	show progress of downloading and parsing

Value

A named vector of pathway titles. The names of the vector are the pathway KEGG IDs.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[keggPathwayGraphs](#)

Examples

```
kpn <- keggPathwayNames("hsa")

# to update the pathway cache for human run:
# kpn <- keggPathwayNames("hsa", updateCache = TRUE)
# this is time consuming and depends on the available bandwidth.

head(kpn)
```

---

nodeWeights *Retrieve the node weights of a graph*

Description

A generic function that returns the node weights of a graph. If index is specified, only the weights of the specified nodes are returned. The user can control which node attribute is interpreted as the weight.

Arguments

object	A graph, any object that inherits the graph class.
index	If supplied, a character or numeric vector of node names or indices.
...	Unused.
attr	The name of the node attribute to use as a weight. You can view the list of defined node attributes and their default values using nodeDataDefaults.
default	The value to use if object has no node attribute named by the value of attr. The default is the value 1.

Details

The weights of all nodes identified by the index are returned. If index is not supplied, the weights of all nodes are returned.

By default, nodeWeights looks for an node attribute with name "weight" and, if found, uses these values to construct the node weight vector. You can make use of attributes stored under a different name by providing a value for the attr argument. For example, if object is a graph instance with an node attribute named "WTS", then the call nodeWeights(object, attr="WTS") will attempt to use those values.

If the graph instance does not have an node attribute with name given by the value of the attr argument, default will be used as the weight for all nodes. Note that if there is an attribute named by attr, then its default value will be used for nodes not specifically customized. See nodeData and nodeDataDefaults for more information.

Value

A named vector with the node weights. The names of the vector are the names of the specified index, or all nodes if index was not provided.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[nodes](#), [nodeData](#)

Examples

```
library(graph)
V <- LETTERS[1:4]
g <- graphNEL(nodes = V, edgemode = "directed")
nodeWeights(g)
nodeWeights(g, "B")
nodeWeights(g, attr = "WT", default = 3)
```

---

pe   *Pathway-Express: Pathway analysis of signaling pathways*

Description

Pathway-Express: Pathway analysis of signaling pathways

Usage

```
pe(x, graphs, ref = NULL, nboot = 2000, verbose = TRUE,
   cluster = NULL, seed = NULL)
```

Arguments

x	named vector of log fold changes for the differentially expressed genes; names(x) must use the same id's as ref and the nodes of the graphs
graphs	list of pathway graphs as objects of type graph (e.g., [graphNEL](#)); the graphs must be weighted graphs (i.e., have an attribute weight for both nodes and edges)
ref	the reference vector for all genes in the analysis; if the reference is not provided or it is identical to names(x) a cut-off free analysis is performed
nboot	number of bootstrap iterations
verbose	print progress output
cluster	a cluster object created by makeCluster for parallel computations
seed	an integer value passed to set.seed() during the boostrap permutations

Details

See details in the cited articles.

Value

An object of class [peRes](#).

Author(s)

Calin Voichita and Sorin Draghici

References

Voichita C., Donato M., Draghici S.: "Incorporating gene significance in the impact analysis of signaling pathways", IEEE Machine Learning and Applications (ICMLA), 2012 11th International Conference on, Vol. 1, p.126-131, 2012

Tarca AL., Draghici S., Khatri P., Hassan SS., Kim J., Kim CJ., Kusanovic JP., Romero R.: "A Signaling Pathway Impact Analysis for Microarray Experiments", 2008, Bioinformatics, 2009, 25(1):75-82.

Khatri P., Draghici S., Tarca AL., Hassan SS., Romero R.: "A system biology approach for the steady-state analysis of gene signaling networks". Progress in Pattern Recognition, Image Analysis and Applications, Lecture Notes in Computer Science. 4756:32-41, November 2007.

Draghici S., Khatri P., Tarca A.L., Amin K., Done A., Voichita C., Georgescu C., Romero R.: "A systems biology approach for pathway level analysis". Genome Research, 17, 2007.

See Also

[Summary](#), [plot.peRes](#), [keggPathwayGraphs](#), [setNodeWeights](#), [setEdgeWeights](#)

Examples

```
# load a multiple sclerosis study (public data available in Array Express
# ID: E-GEOD-21942)
# This file contains the top table, produced by the limma package with
# added gene information. All the probe sets with no gene associate to them,
# have been removed. Only the most significant probe set for each gene has been
# kept (the table is already ordered by p-value)
# The table contains the expression fold change and signficance of each
# probe set in peripheral blood mononuclear cells (PBMC) from 12 MS patients
# and 15 controls.
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
head(top)

# select differentially expressed genes at 1% and save their fold change in a
# vector fc and their p-values in a vector pv
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]

pv <- top$P.Value[top$adj.P.Val <= .01]
names(pv) <- top$entrez[top$adj.P.Val <= .01]

# alternativly use all the genes for the analysis
# NOT RUN:
# fc <- top$logFC
```

```
# names(fc) <- top$entrez

# pv <- top$P.Value
# names(pv) <- top$entrez

# get the reference
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")

# set the beta information (see the citated documents for meaning of beta)
kpg <- setEdgeWeights(kpg)

# inlcude the significance information in the analysis (see Voichita:2012
# for more information)
# set the alpha information based on the pv with one of the predefined methods
kpg <- setNodeWeights(kpg, weights = alphaMLG(pv), defaultWeight = 1)

# perform the pathway analysis
# in order to obtain accurate results the number of boostraps, nboot, should
# be increase to a number like 2000
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

# obtain summary of results
head(Summary(peRes))
```

---

peEdgeRenderInfo   *Extract edge render information from a* pePathway *object*

Description

Extract edge render information from a pePathway object

Usage

```
peEdgeRenderInfo(x, pos.col = "black", pos.lty = "solid",
   pos.ah = "vee", neg.col = "black", neg.lty = "dashed",
   neg.ah = "tee", zero.col = "lightgray",
   zero.lty = "dotted", zero.ah = "none")
```

Arguments

x	an object of class [pePathway](#)
pos.col	color of the edges with possitive weight
pos.lty	line type of the edges with possitive weight
pos.ah	arrow head of the edges with possitive weight
neg.col	color of the edges with negative weight

neg.lty	line type of the edges with negative weight
neg.ah	arrow head of the edges with negative weight
zero.col	color of the edges with zero weight
zero.lty	color of the edges with zero weight
zero.ah	color of the edges with zero weight

Author(s)

Calin Voichita and Sorin Draghici

See Also

[edgeRenderInfo,par](#)

Examples

```
# load experiment
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")
kpg <- setEdgeWeights(kpg)
kpg <- setNodeWeights(kpg, defaultWeight = 1)

# perform the pathway analysis
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

p <- peRes@pathways[[50]]
g <- layoutGraph(p@map, layoutType = "dot")
graphRenderInfo(g) <- list(fixedsize = FALSE)
edgeRenderInfo(g) <- peEdgeRenderInfo(p)
nodeRenderInfo(g) <- peNodeRenderInfo(p)
# notice the different type of edges in the graph (solid/dashed/dotted)
renderGraph(g)
```

---

peNodeRenderInfo   *Extract node render information from a* pePathway *object*

Description

Extract node render information from a pePathway object

Usage

```
peNodeRenderInfo(x, y = "Pert", input.shape = "box",
  default.shape = "ellipse", pos.col = "red",
  neg.col = "blue", zero.col = "white")
```

Arguments

x	an object of class pePathway
y	a string representing the factor to be represented (Pert, Acc or input; see pePathway)
input.shape	shape of nodes that have measured expression change
default.shape	shape of all other nodes
pos.col	color of nodes with a positive y factor
neg.col	color of nodes with a negative y factor
zero.col	color of nodes with the y factor equal to zero

Author(s)

Calin Voichita and Sorin Draghici

See Also

nodeRenderInfo,par

Examples

```
# load experiment
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")
kpg <- setEdgeWeights(kpg)
kpg <- setNodeWeights(kpg, defaultWeight = 1)

# perform the pathway analysis
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

p <- peRes@pathways[[50]]
g <- layoutGraph(p@map, layoutType = "dot")
graphRenderInfo(g) <- list(fixedsize = FALSE)
edgeRenderInfo(g) <- peEdgeRenderInfo(p)
nodeRenderInfo(g) <- peNodeRenderInfo(p)
# notice the different type of nodes in the graph (box/circle)
# the color of each node represents the perturbation (red = positive, blue = negative)
# the shade represents the stregth of the perturbation
renderGraph(g)
```

```
nodeRenderInfo(g) <- peNodeRenderInfo(p, "Acc")
# now, the color of each node represents the accumulation (red = positive, blue = negative)
# notice that square nodes with no parents have no accumulation
renderGraph(g)
```

---

pePathway   *Class that encodes the result of Pathway-Express for a single pathway*

Description

Class that encodes the result of Pathway-Express for a single pathway

Slots

map: an object of type graph (e.g., graphNEL).

input: named vector of fold changes for genes on this pathway. The names of the genes are the orignal IDS used in the analysis

ref: vector of reference IDs on this pathway

boot: an object of class boot encoding the bootstrap information.

Pert: the gene perturbation factors for all genes on the pathway, as computed by Pathway-Express.

Acc: the gene accumulations for all genes on the pathway, as computed by Pathway-Express.

Author(s)

Calin Voichita and Sorin Draghici

See Also

pe, peRes

---

peRes   *Pathway-Express result class*

Description

This class is used to encode the results of the pathway analysis performed by the function pe.

Details

The slots input and ref record global information related to the whole analysis, while the pathways slot records the specific results as pePathway for each one of the pathways used in the analysis.

Slots

pathways: A list of [pePathway](#) objects.

input: named vector of fold changes used for the analysis. The names of the vector are the IDs originaly used.

ref: character vector containing the IDs used as reference in the analysis.

cutOffFree: boolean value indicating if a cut-of-free analysis has been performed.

Author(s)

Calin Voichita and Sorin Draghici

See Also

[pe](#), [pePathway](#)

---

plot.pePathway   *Plot pathway level statistics*

Description

Display graphical representation of pathway level statistic like: i) two way comparison between the measured expression change and one of the factors computed by Pathway-Express ([pe](#)) or ii) the boostrap statistics of the same factors.

Arguments

x	an object of type [pePathway](#)
y	if provided, the factor to be ploted (either Acc (default) or Pert; see [pePathway](#))
...	Arguments to be passed to methods, such as [par](#)
type	type of plot (either two.way (default) or boot)
eps	any value smaller than this will be ploted as 0

Author(s)

Calin Voichita and Sorin Draghici

See Also

[pe](#), [plot.peRes](#), [peNodeRenderInfo](#), [peEdgeRenderInfo](#)

Examples

```
# load experiment
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")
kpg <- setEdgeWeights(kpg)
kpg <- setNodeWeights(kpg, defaultWeight = 1)

# perform the pathway analysis (for more accurate results use nboot = 2000)
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

plot(peRes@pathways[[50]])

plot(peRes@pathways[[50]], "Pert", main = "Perturbation factor")

plot(peRes@pathways[[50]], type = "boot")

plot(peRes@pathways[[50]], "Pert", type = "boot", main = "Perturbation factor")
```

---

plot.peRes	*Plot Pathway-Express result*

Description

Display a two-way plot using two of the p-values from the Pathway-Express analysis.

Arguments

x	an object of type [peRes](#)
y	vector of two p-values names to be combined using comb.pv.func (default: c("pAcc", "pORA")).
...	Arguments to be passed to methods, such as [par](#).
comb.pv.func	the function to combine the p-values - takes as input a vector of p-values and returns the combined p-value (default: [compute.fisher](#)).
adjust.method	the name of the method to adjust the p-value (see [p.adjust](#))
threshold	corrected p-value threshold
eps	any value smaller than this will be considered as eps (default: 1e-6).

Author(s)

Calin Voichita and Sorin Draghici

See Also

pe, Summary.peRes, plot.pePathway

Examples

```
# load experiment
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")
kpg <- setEdgeWeights(kpg)
kpg <- setNodeWeights(kpg, defaultWeight = 1)

# perform the pathway analysis (for more accurate results use nboot = 2000)
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

plot(peRes)

plot(peRes, c("pPert","pORA"), comb.pv.func = compute.normalInv, threshold = .01)
```

---

setEdgeWeights   *Set gene weights based on edge type*

Description

setEdgeWeights

Usage

```
  setEdgeWeights(graphList, edgeTypeAttr = "subtype",
   edgeWeightByType = list(activation = 1, inhibition = -1, expression = 1, repression = -1),
     defaultWeight = 0, combineWeights = sum,
     nodeOnlyGraphs = FALSE)
```

Arguments

graphList   a list of graphNEL objects

edgeTypeAttr   edge attribute to be considered as the edge type. If the edge has multiple types,
                   the edge type attribute is considered as a comma separeted list of types

edgeWeightByType
                   named list of weigths, where the names of the list are the edge type (values of
                   the attribute defined by edgeTypeAttr)

defaultWeight   default value for an edge with a type not defined in edgeWeightByType

combineWeights	for the edges with multiple types, the function to be applied on the vector of weights
nodeOnlyGraphs	boolean value marking if graphs with no edges should be returned or not; note that graphs with all edge weights equal to 0 are considered node only graphs

Value

The `graphList` with the edge weights set.

Author(s)

Calin Voichita and Sorin Draghici

Examples

```
# load the set of pathways
kpg <- keggPathwayGraphs("hsa")

kpg <- setEdgeWeights(kpg)

edgeWeights(kpg[["path:hsa04110"]])
```

---

setNodeWeights   *Set node weights*

Description

Set node weights

Usage

```
setNodeWeights(graphList, weights = NULL,
    defaultWeight = 1)
```

Arguments

graphList	a list of graph (e.g., [graphNEL](#)) objects
weights	named vector or matrix; if vector, the node is going to have the same weight in all graphs it appears; if matrix, the rows represent nodes and columns represent graphs and the node will have different weights in each pathway
defaultWeight	the default weight for all nodes not set by the parameter `weights`

Value

The `graphList` with the node weights set.

Author(s)

Calin Voichita and Sorin Draghici

Examples

```
# load the set of pathways
kpg <- keggPathwayGraphs("hsa")

kpg <- setNodeWeights(kpg)

nodeWeights(kpg[["path:hsa04110"]])
```

Summary   *Summarize the results of a Pathway-Express analysis*

Description

Summarize the results of a Pathway-Express analysis

Arguments

x	Pathways-Express result object obtained using pe
pathNames	named vector of pathway names; the names of the vector are the IDs of the pathways
totalAcc	boolean value indicating if the total accumulation should be computed
totalPert	boolean value indicating if the total perturbation should be computed
normalize	boolean value indicating if normalization with regards to the boostrap simulations should be performed on totalAcc and totalPert
pPert	boolean value indicating if the significance of the total perturbation in regards to the bootstrap permutations should be computed
pAcc	boolean value indicating if the significance of the total accumulation in regards to the bootstrap permutations should be computed
pORA	boolean value indicating if the over-represtation p-value should be computed
comb.pv	vector of the p-value names to be combine (any of the above p-values)
comb.pv.func	the function to combine the p-values; takes as input a vector of p-values and returns the combined p-value
order.by	the name of the p-value that is used to order the results
adjust.method	the name of the method to adjust the p-value (see p.adjust)

See Also

pe

Examples

```
# load experiment
load(system.file("extdata/E-GEOD-21942.topTable.RData", package = "ROntoTools"))
fc <- top$logFC[top$adj.P.Val <= .01]
names(fc) <- top$entrez[top$adj.P.Val <= .01]
ref <- top$entrez

# load the set of pathways
kpg <- keggPathwayGraphs("hsa")
kpg <- setEdgeWeights(kpg)
kpg <- setNodeWeights(kpg, defaultWeight = 1)

# perform the pathway analysis
peRes <- pe(fc, graphs = kpg, ref = ref, nboot = 100, verbose = TRUE)

# obtain summary of results
head(Summary(peRes))

kpn <- keggPathwayNames("hsa")

head(Summary(peRes))

head(Summary(peRes, pathNames = kpn, totalAcc = FALSE, totalPert = FALSE,
             pAcc = FALSE, pORA = FALSE, comb.pv = NULL, order.by = "pPert"))
```

Index