Package 'graphite'

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Title GRAPH Interaction from pathway Topological Environment

Description Graph objects from pathway topology derived from KEGG, Panther, PathBank, PharmGKB, Reactome SMPDB and WikiPathways databases.

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URL https://github.com/sales-lab/graphite

BugReports https://github.com/sales-lab/graphite/issues

Depends R (>= 4.2), methods

Imports AnnotationDbi, graph (>= 1.67.1), httr, rappdirs, stats, utils, graphics, rlang, purrr

Suggests checkmate, a4Preproc, ALL, BiocStyle, clipper, codetools, hgu133plus2.db, hgu95av2.db, impute, knitr, org.Hs.eg.db, parallel, R.rsp, RCy3, rmarkdown, SPIA (>= 2.2), testthat, topologyGSA (>= 1.4.0)

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R topics documented:

`as.list.PathwayList` *Convertion of PathwayLists into lists.*

Description

Converts a `PathwayList` into a list of `Pathway`s.

Usage

```
  ## S3 method for class 'PathwayList'
as.list(x, ...)
```

Arguments

`x`	a `PathwayList` object
`...`	extra arguments to as.list

Value

A list of pathways.

Author(s)

Gabriele Sales

See Also

`PathwayList`

Examples

```
as.list(pathways("hsapiens", "kegg"))
```

`buildPathway` *Build a Pathway object.*

Description

This function creates a new object of type `Pathway` given a data frame describing its edges.

Usage

```
buildPathway(id, title, species, database, proteinEdges,
             metaboliteEdges = NULL, mixedEdges = NULL,
             timestamp = NULL)
```

Arguments

`id`	the pathway identifier.
`title`	the title of the pathway.
`species`	the species the pathway belongs to.
`database`	the name of the database the pathway derives from.
`proteinEdges`	a data.frame of edges between proteins (or genes). Must have the following columns: src_type, src, dest_type, dest, direction and type. Direction must be one of the two strings: "directed" or "undirected".
`metaboliteEdges`	interactions between metabolites. Can be `NULL`. Otherwise, it must have the same structure as `proteinEdges`.
`mixedEdges`	interactions between metabolites and proteins. Can be `NULL`. Otherwise, it must have the same structure as `proteinEdges`.
`timestamp`	when the pathway was annotated, by default the time `buildPathway` is called.

Value

A new `Pathway` instance.

Examples

```
edges <- data.frame(src_type = "ENTREZID", src="672",
                    dest_type = "ENTREZID", dest="7157",
                    direction="undirected", type="binding")
pathway <- buildPathway("#1", "example", "hsapiens", "database", edges)

# Example with metabolites:
edges <- data.frame(src_type = "ENTREZID", src="672",
                    dest_type = "ENTREZID", dest="7157",
                    direction="undirected", type="binding")
mixed <- data.frame(src_type = "CHEBI", src="77750",
                    dest_type = "ENTREZID", dest="7157",
                    direction="undirected", type="binding")
pathway <- buildPathway("#1", "example", "hsapiens", "database",
                        edges, mixedEdges = mixed)
```

`convertIdentifiers` *Convert the node identifiers of a pathway.*

Description

Converts the node identifiers of pathways.

If the option `Ncpus` is set to a value larger than 1 and the package `parallel` is installed, the conversion procedure will automatically use multiple cores.

Usage

```
convertIdentifiers(x, to)
```

Arguments

`x`	can be a list of pathways or a single pathway
`to`	a string describing the type of the identifier. Can assume the values `"entrez"`, `"symbol"` or the name of one of the columns provided by an Annotation package (for example, `"UNIPROT"`).

Value

A `Pathway` object.

See Also

`Pathway`

Examples

```
r <- pathways("hsapiens", "reactome")
convertIdentifiers(r$`mTORC1-mediated signalling`, "symbol")
```

cytoscapePlot *Plot a pathway graph in Cytoscape*

Description

Renders the topology of a pathway as a Cytoscape graph.

Usage

```
cytoscapePlot(pathway, ..., cy.ver = 3)
```

Arguments

pathway	a Pathway object.
...	optional arguments forwarded to pathwayGraph.
cy.ver	select a Cytoscape version. Only version 3 is supported in this release.

Details

Requires the RCy3 package.

Value

An invisible list with two items:

graph	the graphNEL object sent to Cytoscape.
suid	the RCy3 network SUID.

See Also

Pathway

pathwayGraph

Examples

```
## Not run:
  r <- pathways()
  cytoscapePlot(convertIdentifiers(reactome$`Unwinding of DNA`, "symbol"))

## End(Not run)
```

Pathway-class *Class* "Pathway"

Description

A biological pathway.

Variants

A Pathway instance actually stores multiple variants of the same biological data.

This is the list of included variants:

- proteins: includes only interactions among proteins;
- metabolites: includes only interactions among metabolites;
- mixed: includes all available interactions.

Methods

pathwayId(p): Returns the native ID of the pathway.

pathwayTitle(p): Returns the title of the pathway.

pathwayDatabase(p): Returns the name of the database the pathway was derived from.

pathwaySpecies(p): Returns the name of the species in which the pathway was annotated.

pathwayTimestamp(p): Returns the date of pathway data retrieval.

pathwayURL(p): Returns the URL of the pathway in its original database, if available.

convertIdentifiers(p, to): Returns a new pathway using a different type of node identifiers.

edges(p, which = c("proteins", "metabolites", "mixed"), stringsAsFactors = TRUE): Returns a data.frame describing the edges of this pathway.
The option which selects the desired pathway variant (see section "Variants" above).
If stringsAsFactors is TRUE, strings are converted to factors.

nodes(p, which = c("proteins", "metabolites", "mixed")): Returns the names of the nodes belonging to this pathway.
The option which selects the desired pathway variant (see section "Variants" above).

plot(p): Shows the pathway topology in Cytoscape.

runClipper(p, expr, classes, method, ...): Runs a clipper analysis over the pathway.

runTopologyGSA(p, test, exp1, exp2, alpha, ...): Runs a topologyGSA analysis over the pathway.

Author(s)

Gabriele Sales

See Also

pathways

Examples

```
reactome <- pathways("hsapiens", "reactome")
pathway <- reactome[[1]]

pathwayTitle(pathway)
pathwaySpecies(pathway)
nodes(pathway)
edges(pathway)
```

`pathwayDatabases` *List the available pathway databases.*

Description

Obtains the list of pathway databases available through `graphite`.

Usage

```
pathwayDatabases()
```

Value

Returns a `data.frame` with two columns: `species` and `database`.

Author(s)

Gabriele Sales

See Also

`pathways`

Examples

```
pathwayDatabases()
```

pathwayGraph *Graph representing the topology of a pathway*

Description

Builds a graphNEL object representing the topology of a pathway.

Usage

```
pathwayGraph(pathway, which = "proteins", edge.types = NULL)
```

Arguments

pathway	a Pathway object.
which	the pathway variant you want. See Pathway documentation for a list of the supported variants.
edge.types	keep only the edges maching the type names in this vector.

Value

A graphNEL object.

See Also

Pathway

graphNEL

Examples

```
r <- pathways("hsapiens", "reactome")
pathwayGraph(r$`mTORC1-mediated signalling`, edge.types="Binding")
```

PathwayList-class *Class "PathwayList"*

Description

A collection of pathways from a single database.

Extends

Class "Pathways", directly.

Methods

`l[i]` returns a selection of the pathways contained in the pathway list.

`l[[i]]` gives access to one of the pathways contained in the pathway list.

`l$‘title‘` loads a pathways by its title.

`convertIdentifiers(l, to)` returns a new list of pathways using a different type of node identifiers.

`length(l)` returns the number of pathways contained in the list.

`names(l)` returns the titles of the pathways contained in the list.

`prepareSPIA(l, pathwaySetName, print.names=FALSE)` prepares the pathways for a SPIA analysis.

`runClipper(l, expr, classes, method, maxNodes=150, ...)` runs a `clipper` analysis over all the pathways in the list.

`runTopologyGSA(l, test, exp1, exp2, alpha, maxNodes=150, ...)` runs a `topologyGSA` analysis over all the pathways in the list.

Author(s)

Gabriele Sales

See Also

`pathways`

`pathways` *Retrieve a list of pathways.*

Description

Retrieve a list of pathways from a database for a given species.

graphite currently supports the following databases:

- KEGG
- PANTHER
- PathBank
- PharmGKB
- Reactome
- SMPDB
- WikiPathways

Call the `pathwayDatabase` function for more details.

Usage

```
pathways(species, database)
```

Arguments

species	one of the supported species
database	the name of the pathway database

Value

A PathwayList object.

See Also

PathwayList, pathwayDatabases

Examples

```
pathways("hsapiens", "reactome")
```

Pathways-class *Class* "Pathways"

Description

A virtual class acting as a common parent to all other classes representing pathway databases.

Objects from the Class

A virtual Class: No objects may be created from it.

Methods

No methods defined with class "Pathways" in the signature.

Author(s)

Gabriele Sales

See Also

PathwayList

prepareSPIA *Prepare pathway dataset needed by runSPIA.*

Description

Prepare pathway dataset needed by runSPIA. See runSPIA and spia for more details.

Usage

```
prepareSPIA(db, pathwaySetName, print.names = FALSE)
```

Arguments

db	a PathwayList object or a list of Pathways.
pathwaySetName	name of the output pathway set.
print.names	print pathway names as the conversion advances.

Value

This function has no return value.

References

Tarca AL, Draghici S, Khatri P, Hassan SS, Mittal P, Kim JS, Kim CJ, Kusanovic JP, Romero R. A novel signaling pathway impact analysis. Bioinformatics. 2009 Jan 1;25(1):75-82.

Adi L. Tarca, Sorin Draghici, Purvesh Khatri, et. al, A Signaling Pathway Impact Analysis for Microarray Experiments, 2008, Bioinformatics, 2009, 25(1):75-82.

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

runSPIA

spia

PathwayList

runClipper *Run a topological analysis on an expression dataset using clipper.*

Description

clipper is a package for topological gene set analysis. It implements a two-step empirical approach based on the exploitation of graph decomposition into a junction tree to reconstruct the most relevant signal path. In the first step clipper selects significant pathways according to statistical tests on the means and the concentration matrices of the graphs derived from pathway topologies. Then, it "clips" the whole pathway identifying the signal paths having the greatest association with a specific phenotype.

If the option `Ncpus` is set to a value larger than 1 and the package `parallel` is installed, the conversion procedure will automatically use multiple cores.

Usage

```
runClipper(x, expr, classes, method, which = "proteins", seed = NULL, ...)
```

Arguments

`x`	a `PathwayList`, a list of `Pathway`s or a single `Pathway` object.
`expr`	a `matrix` (size: number `p` of genes x number `n` of samples) of gene expression.
`classes`	a `vector` (length: `n`) of class assignments.
`method`	the kind of test to perform on the cliques. It could be either `"mean"` or `"variance"`.
`which`	the pathway variant you want. See `Pathway` documentation for a list of the supported variants.
`seed`	if not `NULL`, set the seed for the random number generator used by clipper.
`...`	additional options: see for details `easyClip`. When invoked on a `PathwayList`, you can use the named option `maxNodes` to limit the analysis to those pathways with at most a given number of nodes.

Details

The expression data and the pathway have to be annotated in the same set of identifiers.

Value

See the documentation of `easyClip`.

References

Martini P, Sales G, Massa MS, Chiogna M, Romualdi C. Along signal paths: an empirical gene set approach exploiting pathway topology. Nucleic Acids Res. 2013 Jan 7;41(1):e19. doi: 10.1093/nar/gks866. Epub 2012 Sep 21. PubMed PMID: 23002139; PubMed Central PMCID: PMC3592432.

See Also

clipper

Examples

```
if (require(clipper) & require(ALL) & require(a4Preproc)) {
  data(ALL)
  pheno <- as(phenoData(ALL), "data.frame")
  samples <- unlist(lapply(c("NEG", "BCR/ABL"), function(t) {
    which(grepl("^B\\d*", pheno$BT) & (pheno$mol.biol == t))[1:10]
  }))
  classes <- c(rep(1,10), rep(2,10))

  expr <- exprs(ALL)[,samples]
  rownames(expr) <- paste("ENTREZID", featureData(addGeneInfo(ALL))$ENTREZID,
                          sep = ":")

  k <- as.list(pathways("hsapiens", "kegg"))
  selected <- k[c("Bladder cancer", "Hippo signaling pathway - multiple species")]

  runClipper(selected, expr, classes, "mean", pathThr = 0.1)
}
```

---

runSPIA *Run SPIA analysis*

Description

Run a topological analysis on an expression dataset using SPIA.

Usage

```
runSPIA(de, all, pathwaySetName, ...)
```

Arguments

de	A named vector containing log2 fold-changes of the differentially expressed genes. The names of this numeric vector are Entrez gene IDs.
all	A vector with the Entrez IDs in the reference set. If the data was obtained from a microarray experiment, this set will contain all genes present on the specific array used for the experiment. This vector should contain all names of the 'de' argument.
pathwaySetName	The name of a pathway set created with prepareSPIA.
...	Additional options to pass to spia.

Details

The spia option "organism" is internally used. It is an error use it in the additional options.

Value

The same of spia, without KEGG links. A data frame containing the ranked pathways and various statistics: pSize is the number of genes on the pathway; NDE is the number of DE genes per pathway; tA is the observed total preturbation accumulation in the pathway; pNDE is the probability to observe at least NDE genes on the pathway using a hypergeometric model; pPERT is the probability to observe a total accumulation more extreme than tA only by chance; pG is the p-value obtained by combining pNDE and pPERT; pGFdr and pGFWER are the False Discovery Rate and respectively Bonferroni adjusted global p-values; and the Status gives the direction in which the pathway is perturbed (activated or inhibited).

References

Tarca AL, Draghici S, Khatri P, Hassan SS, Mittal P, Kim JS, Kim CJ, Kusanovic JP, Romero R. A novel signaling pathway impact analysis. Bioinformatics. 2009 Jan 1;25(1):75-82.

Adi L. Tarca, Sorin Draghici, Purvesh Khatri, et. al, A Signaling Pathway Impact Analysis for Microarray Experiments, 2008, Bioinformatics, 2009, 25(1):75-82.

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

spia

Examples

```
if (require(SPIA) && require(hgu133plus2.db)) {
  data(colorectalcancer)

  top$ENTREZ <- mapIds(hgu133plus2.db, top$ID, "ENTREZID", "PROBEID", multiVals = "first")
  top <- top[!is.na(top$ENTREZ) & !duplicated(top$ENTREZ), ]
  top$ENTREZ <- paste("ENTREZID", top$ENTREZ, sep = ":")
  tg1 <- top[top$adj.P.Val < 0.05, ]

  DE_Colorectal = tg1$logFC
  names(DE_Colorectal) <- tg1$ENTREZ
  ALL_Colorectal <- top$ENTREZ

  kegg <- pathways("hsapiens", "kegg")[1:20]
  kegg <- convertIdentifiers(kegg, "ENTREZID")
  prepareSPIA(kegg, "keggEx")
  runSPIA(de = DE_Colorectal, all = ALL_Colorectal, "keggEx")

  unlink("keggExSPIA.RData")
}
```

`runTopologyGSA` *Run a topological analysis on an expression dataset using topologyGSA.*

Description

Use graphical models to test the pathway components highlighting those involved in its deregulation.

If the option `Ncpus` is set to a value larger than 1 and the package `parallel` is installed, the conversion procedure will automatically use multiple cores.

Usage

```
runTopologyGSA(x, test, exp1, exp2, alpha, ...)
```

Arguments

`x`	a `PathwayList`, a list of `Pathway`s or a single `Pathway` object.
`test`	Either `"var"` and `"mean"`. Determine the type of test used by topologyGSA.
`exp1`	Experiment matrix of the first class, genes in columns.
`exp2`	Experiment matrix of the second class, genes in columns.
`alpha`	Significance level of the test.
`...`	Additional parameters forwarded to `topologyGSA`. When invoked on a `PathwayList`, can use the named option "maxNodes" to limit the analysis to those pathways having up to this given number of nodes.

Details

This function produces a warning and returns NULL when the number of genes in common between the expression matrices and the pathway is less than 3.

Value

See documentation of `pathway.var.test` and `pathway.mean.test`.

References

Massa MS, Chiogna M, Romualdi C. Gene set analysis exploiting the topology of a pathway. BMC System Biol. 2010 Sep 1;4:121.

Examples

```
if (require(topologyGSA)) {
  data(examples)
  colnames(y1) <- paste("SYMBOL", colnames(y1), sep = ":")
  colnames(y2) <- paste("SYMBOL", colnames(y2), sep = ":")

  k <- pathways("hsapiens", "kegg")
  p <- convertIdentifiers(k[["Fc epsilon RI signaling pathway"]], "SYMBOL")
  runTopologyGSA(p, "var", y1, y2, 0.05)
}
```

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