

## Package: ReactomePA (via r-universe)

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Type Package

**Title** Reactome Pathway Analysis**Version** 1.99.2

**Maintainer** Guangchuang Yu <guangchuangyu@gmail.com>

**Description** This package provides functions for pathway analysis based on REACTOME pathway database. It implements enrichment analysis, gene set enrichment analysis, network-based enrichment analysis (NSEA) on the Reactome reaction graph, Bayesian term selection, weighted enrichment, and several functions for visualization. This package is not affiliated with the Reactome team.

**Depends** R (>= 3.4.0)

**Imports** AnnotationDbi, enrichplot, enrichit (>= 0.2.2), ggplot2 (>= 3.3.5), ggraph, reactome.db, igraph, graphite, gson, Matrix, utils, yulab.utils (>= 0.1.5)

**Suggests** clusterProfiler, knitr, rmarkdown, org.Hs.eg.db, prettydoc, testthat

## VignetteBuilder knitr

**ByteCompile** true

**License** GPL-2

**URL** <https://yulab-smu.top/contribution-knowledge-mining/>

**BugReports** <https://github.com/GuangchuangYu/ReactomePA/issues>

**biocViews** Pathways, Visualization, Annotation, MultipleComparison, GeneSetEnrichment, Reactome

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|                |                                                                |
|----------------|----------------------------------------------------------------|
| bayes_reactome | <i>Bayesian term selection for Reactome enrichment results</i> |
|----------------|----------------------------------------------------------------|

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**Description**

‘bayes\_reactome()’ adds a model-based selection layer on top of ‘enrichPathway()’ results. It estimates the posterior probability that each candidate Reactome pathway is an active biological program explaining the observed input genes.

**Usage**

```
bayes_reactome(  
  x,  
  candidate = c("top", "significant", "all"),  
  n_terms = 200,  
  by = "p.adjust",  
  prior = 0.1,  
  false_positive = 0.01,  
  false_negative = 0.1,  
  n_iter = 5000,  
  burnin = 1000,  
  thin = 1,  
  posterior_cutoff = 0.5,  
  seed = NULL,  
  verbose = FALSE  
)
```

**Arguments**

|                               |                                                                                                                                                                                                         |
|-------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>x</code>                | An 'enrichResult' object from 'enrichPathway()'.                                                                                                                                                        |
| <code>candidate</code>        | Candidate terms to include. "significant" uses 'as.data.frame(x)', "all" uses 'x@result', "top" uses the top 'n_terms' rows from 'x@result' ordered by 'by'; or provide a character vector of term IDs. |
| <code>n_terms</code>          | Maximum number of candidate terms when 'candidate = "top"' or when more candidates are supplied than this value. Use 'Inf' to disable.                                                                  |
| <code>by</code>               | Column used to order candidate terms.                                                                                                                                                                   |
| <code>prior</code>            | Prior probability that a term is active.                                                                                                                                                                |
| <code>false_positive</code>   | Probability of observing a gene not covered by active terms.                                                                                                                                            |
| <code>false_negative</code>   | Probability of missing a gene covered by active terms.                                                                                                                                                  |
| <code>n_iter</code>           | Total number of MCMC iterations.                                                                                                                                                                        |
| <code>burnin</code>           | Number of initial iterations discarded.                                                                                                                                                                 |
| <code>thin</code>             | Keep one sample every 'thin' iterations after burn-in.                                                                                                                                                  |
| <code>posterior_cutoff</code> | Terms with posterior greater than or equal to this value are marked active.                                                                                                                             |
| <code>seed</code>             | Optional random seed.                                                                                                                                                                                   |
| <code>verbose</code>          | Print sampler progress.                                                                                                                                                                                 |

**Details**

This is a thin wrapper around 'enrichit::bayes\_enrich()', intended as a result-compression and interpretation layer for Reactome pathway enrichment. Reactome's hierarchical pathway structure often produces many redundant significant terms — Bayesian selection helps distinguish truly active programs from statistically significant but dependent ones.

**Value**

The input 'enrichResult' object with additional columns in '@result': 'posterior', 'posterior\_odds', 'bayes\_rank', 'bayes\_active', 'bayes\_covered\_gene', and 'bayes\_covered\_count'.

**See Also**

[enrichit::bayes\_enrich()]

**Examples**

```
## Not run:
gene <- c("11171", "8243", "112464", "2194",
          "9318", "79026", "1654", "65003",
          "6240", "3476", "6238", "3836",
          "4176", "1017", "249")
x <- enrichPathway(gene, pvalueCutoff = 0.1)
bx <- bayes_reactome(x)
head(as.data.frame(bx))

## End(Not run)
```

---

|         |                                                       |
|---------|-------------------------------------------------------|
| DataSet | <i>Datasets sample contains a sample of gene IDs.</i> |
|---------|-------------------------------------------------------|

---

### Description

Datasets sample contains a sample of gene IDs.

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|               |                                                                                                                                              |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| enrichPathway | <i>Pathway Enrichment Analysis of a gene set. Given a vector of genes, this function will return the enriched pathways with FDR control.</i> |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------|

---

### Description

Pathway Enrichment Analysis of a gene set. Given a vector of genes, this function will return the enriched pathways with FDR control.

### Usage

```
enrichPathway(
  gene,
  pvalueCutoff = 0.05,
  pAdjustMethod = "BH",
  universe = NULL,
  weight = NULL,
  minGSSize = 10,
  maxGSSize = 500,
  qvalueCutoff = 0.2,
  organism = "human",
  readable = FALSE
)
```

### Arguments

|               |                                                                                                                                                              |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| gene          | a vector of entrez gene id.                                                                                                                                  |
| pvalueCutoff  | Cutoff value of pvalue.                                                                                                                                      |
| pAdjustMethod | one of "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none"                                                                                 |
| universe      | background genes                                                                                                                                             |
| weight        | A named numeric vector of weights for background genes. If provided, Weighted ORA will be performed using Wallenius' noncentral hypergeometric distribution. |
| minGSSize     | minimal size of genes annotated by Ontology term for testing.                                                                                                |
| maxGSSize     | maximal size of each geneSet for analyzing                                                                                                                   |
| qvalueCutoff  | Cutoff value of qvalue                                                                                                                                       |
| organism      | one of "human", "rat", "mouse", "celegans", "yeast", "zebrafish", "fly".                                                                                     |
| readable      | whether mapping gene ID to gene Name                                                                                                                         |

**Value**

A enrichResult instance.

**Author(s)**

Guangchuang Yu <http://ygc.name>

**See Also**

[enrichResult-class](#)

**Examples**

```
## Not run:
gene <- c("11171", "8243", "112464", "2194",
          "9318", "79026", "1654", "65003",
          "6240", "3476", "6238", "3836",
          "4176", "1017", "249")
yy = enrichPathway(gene, pvalueCutoff=0.05)
head(summary(yy))

## End(Not run)
```

---

getDb

*getDb*

---

**Description**

mapping organism name to annotationDb package name

**Usage**

```
getDb(organism)
```

**Arguments**

organism            one of supported organism

**Value**

annotationDb name

**Author(s)**

Yu Guangchuang

gsePathway

*gsePathway***Description**

Gene Set Enrichment Analysis of Reactome Pathway

**Usage**

```

gsePathway(
  geneList,
  organism = "human",
  exponent = 1,
  weight = NULL,
  minGSSize = 10,
  maxGSSize = 500,
  eps = 1e-10,
  pvalueCutoff = 0.05,
  pAdjustMethod = "BH",
  verbose = TRUE,
  nPerm = 1000,
  method = "multilevel",
  adaptive = FALSE,
  minPerm = 101,
  maxPerm = 1e+05,
  pvalThreshold = 0.1,
  seed = FALSE,
  ...
)

```

**Arguments**

|               |                                                                                                                                                                                                 |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| geneList      | order ranked geneList                                                                                                                                                                           |
| organism      | organism                                                                                                                                                                                        |
| exponent      | weight of each step                                                                                                                                                                             |
| weight        | A named numeric vector of weights for genes. The names should match the names of geneList. If provided, the geneList will be multiplied by the weight and resorted before GSEA (default: NULL). |
| minGSSize     | minimal size of each geneSet for analyzing                                                                                                                                                      |
| maxGSSize     | maximal size of each geneSet for analyzing                                                                                                                                                      |
| eps           | boundary for calculating the p value in multilevel mode                                                                                                                                         |
| pvalueCutoff  | pvalue Cutoff                                                                                                                                                                                   |
| pAdjustMethod | pvalue adjustment method                                                                                                                                                                        |
| verbose       | print message or not                                                                                                                                                                            |

|               |                                                                                                                                                                                                                                                                                                                                           |
|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| nPerm         | The number of permutations for the "permute" method                                                                                                                                                                                                                                                                                       |
| method        | one of "sample", "permute", "multilevel"                                                                                                                                                                                                                                                                                                  |
| adaptive      | logical                                                                                                                                                                                                                                                                                                                                   |
| minPerm       | minimal number of permutations for the "multilevel" method                                                                                                                                                                                                                                                                                |
| maxPerm       | maximal number of permutations for the "multilevel" method                                                                                                                                                                                                                                                                                |
| pvalThreshold | The p-value threshold for the "multilevel" method                                                                                                                                                                                                                                                                                         |
| seed          | random seed for reproducibility, set to a number (or TRUE to use a fixed default seed) to make the result reproducible, or FALSE (default) to draw a random seed on each run, so results may vary between runs. The underlying permutation engine uses its own RNG seeded with this value; see <code>enrichit::gsea()</code> for details. |
| ...           | other parameters passed to <code>enrichit::gsea_gson()</code>                                                                                                                                                                                                                                                                             |

**Value**

`gseaResult` object

**Author(s)**

Yu Guangchuang

---

`gson_Reactome`

*`gson_Reactome`*

---

**Description**

download the latest version of Reactome and stored in a 'GSON' object

**Usage**

```
gson_Reactome(organism = "human")
```

**Arguments**

`organism` one of "human", "rat", "mouse", "celegans", "yeast", "zebrafish", "fly".

**Value**

a 'GSON' object

**Examples**

```
## Not run:
rec_gson <- gson_Reactome("human")

## End(Not run)
```

## Description

`nsePathway()` performs network-based set enrichment analysis (NSEA) on Reactome pathways. Instead of using raw gene-level scores directly, scores are propagated across the Reactome reaction graph via Random Walk with Restart (RWR), and enrichment scores are computed on the diffused ranking. Statistical significance is assessed with a whole-pipeline permutation null (gene labels of the input scores are reshuffled, the diffusion is re-run, and the enrichment scores are recomputed), so the reported p-values account for the correlation induced by network diffusion and control the false-positive rate. This captures pathway-level signals that may be diluted in individual gene-level statistics.

## Usage

```
nsePathway(
  geneList,
  organism = "human",
  mode = c("evidence", "signed"),
  network = NULL,
  restart_prob = 0.5,
  specific_weight = FALSE,
  minGSSize = 10,
  maxGSSize = 500,
  threshold = 1e-09,
  maxIter = 100,
  nPerm = 1000,
  seed = NULL,
  verbose = TRUE,
  ...
)
```

## Arguments

|                           |                                                                                                                                                                                                             |
|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>geneList</code>     | A named numeric vector of gene-level scores (e.g. <code>log2FC</code> ). Names must be Entrez Gene IDs.                                                                                                     |
| <code>organism</code>     | Supported organism. Default is "human".                                                                                                                                                                     |
| <code>mode</code>         | Character, either "evidence" (default) or "signed". In "evidence" mode, all seeds are propagated once. In "signed" mode, positive and negative seeds are propagated separately and the difference is taken. |
| <code>network</code>      | Optional pre-built network from <code>prepareReactomeNetwork()</code> . If NULL, the network is auto-built and cached.                                                                                      |
| <code>restart_prob</code> | Restart probability for RWR (default: 0.5).                                                                                                                                                                 |

|                              |                                                                                                                                                                                                                                                                                                                                                                     |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>specific_weight</code> | Logical, whether to apply gene specificity weighting (TF-IDF style). Default is FALSE.                                                                                                                                                                                                                                                                              |
| <code>minGSSize</code>       | Minimal size of each gene set for analyzing (default: 10).                                                                                                                                                                                                                                                                                                          |
| <code>maxGSSize</code>       | Maximal size of each gene set for analyzing (default: 500).                                                                                                                                                                                                                                                                                                         |
| <code>threshold</code>       | Convergence threshold for RWR (default: 1e-9).                                                                                                                                                                                                                                                                                                                      |
| <code>maxIter</code>         | Maximal number of RWR iterations (default: 100).                                                                                                                                                                                                                                                                                                                    |
| <code>nPerm</code>           | Number of whole-pipeline permutations used to estimate p-values and NES (default: 1000). Each permutation reshuffles the gene labels of the input scores, re-runs the RWR diffusion over the network, and recomputes the enrichment scores, giving a null distribution that accounts for the network diffusion. The smallest estimable p-value is $1/(nPerm + 1)$ . |
| <code>seed</code>            | Numeric random seed for the whole-pipeline permutation null (default: NULL uses the current R RNG state). Set a number for fully reproducible results.                                                                                                                                                                                                              |
| <code>verbose</code>         | Print progress messages (default: TRUE).                                                                                                                                                                                                                                                                                                                            |
| <code>...</code>             | Other arguments passed to <code>'enrichit::nsea_gson()'</code> .                                                                                                                                                                                                                                                                                                    |

## Details

The Reactome reaction network is automatically built and cached on first call. Users can pre-build and pass a custom network via the `'network'` parameter.

## Value

A `'nseaResult'` object (inherits from `'gseaResult'`).

## See Also

`[prepareReactomeNetwork()]`, `[enrichit::nsea()]`

## Examples

```
## Not run:
data(geneList, package = "DOSE")
nsea_res <- nsePathway(geneList)
head(nsea_res)

## End(Not run)
```

---

```
prepareReactomeNetwork
```

*Prepare Reactome reaction network for NSEA*

---

## Description

Builds a gene-gene interaction network from all Reactome reaction steps for a given species. Two genes are connected if they co-participate in the same reaction step. The network is returned as a column-normalized sparse matrix (dgCMatrix) suitable for Random Walk with Restart.

## Usage

```
prepareReactomeNetwork(
  organism = "human",
  directed = FALSE,
  cores = getOption("mc.cores", 1L)
)
```

## Arguments

|          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| organism | Supported organism: "human", "mouse", "rat", "yeast", "zebrafish", "fly", "cel-egans", etc. See 'graphite::pathways()' for the full list.                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| directed | Logical. If FALSE (default), edges are treated as undirected (reciprocal edges added).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| cores    | Number of CPU cores used to convert Reactome pathways to reaction edges in parallel. Defaults to 'getOption("mc.cores")', or '1' (serial) if the option is unset: the conversion is fast enough (~40 s for human) that parallelizing is optional, and serial leaves the rest of the machine untouched. The per-pathway conversions are independent and pure in-memory vectorized operations (the species identifier map is loaded once up front), so wall time scales close to linearly with 'cores'. On Windows, 'mclapply()' falls back to serial execution regardless. |

## Details

The network is cached via 'yulab.utils::with\_cache()' so repeated calls are fast.

## Value

A sparse matrix (dgCMatrix) of the Reactome reaction graph.

## Examples

```
## Not run:
net <- prepareReactomeNetwork("human")

## End(Not run)
```

---

|             |                    |
|-------------|--------------------|
| viewPathway | <i>viewPathway</i> |
|-------------|--------------------|

---

**Description**

view reactome pathway

**Usage**

```
viewPathway(  
  pathName,  
  organism = "human",  
  readable = TRUE,  
  foldChange = NULL,  
  keyType = "ENTREZID",  
  layout = "kk"  
)
```

**Arguments**

|            |                                                             |
|------------|-------------------------------------------------------------|
| pathName   | pathway Name                                                |
| organism   | supported organism                                          |
| readable   | logical                                                     |
| foldChange | fold change                                                 |
| keyType    | keyType of gene ID (i.e. names of foldChange, if available) |
| layout     | graph layout                                                |

**Details**

plotting reactome pathway

**Value**

plot

**Author(s)**

Yu Guangchuang

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