Package 'RITAN'

March 26, 2024

Type Package

Title Rapid Integration of Term Annotation and Network resources

Version 1.26.0

Description Tools for comprehensive gene set enrichment and extraction of multi-resource high confidence subnetworks. RITAN facilitates bioinformatic tasks for enabling network biology research.

LazyData TRUE

Depends R (>= 4.0),

Imports graphics, methods, stats, utils, grid, gridExtra, reshape2, gplots, ggplot2, plotrix, RColorBrewer, STRINGdb, MCL, linkcomm, dynamicTreeCut, gsubfn, hash, png, sqldf, igraph, BgeeDB, knitr, RITANdata, GenomicFeatures, ensembldb, AnnotationFilter, EnsDb.Hsapiens.v86

VignetteBuilder knitr

Collate 'lib_enrichment.R' 'lib_network.R' 'interconnectivity_functions.R'

RoxygenNote 7.1.1

Suggests rmarkdown, BgeeDB

License file LICENSE

biocViews QualityControl, Network, NetworkEnrichment, NetworkInference, GeneSetEnrichment, FunctionalGenomics, GraphAndNetwork

NeedsCompilation no

git_url https://git.bioconductor.org/packages/RITAN

git_branch RELEASE_3_18

git_last_commit 13a63fd

git_last_commit_date 2023-10-24

Repository Bioconductor 3.18

Date/Publication 2024-03-25

Author Michael Zimmermann [aut, cre]

Maintainer Michael Zimmermann <mtzimmermann@mcw.edu>

2 as.graph

R topics documented:

| check_any_net_input check_net_input cov_undirected enrichment_symbols geneset_overlap icon_single_within icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichses vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes writeGMT write_simple_table |
|--|
| cov_undirected enrichment_symbols geneset_overlap icon_single_within icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment summary.term_enrichment summary.term |
| enrichment_symbols geneset_overlap icon_single_within icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichdent term_enrichment term_enrichdenent summary.term_enrichdenent sum |
| geneset_overlap icon_single_within icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment_by_subset vac1.dayOvs31.de.genes vac2.dayOvs56.de.genes |
| icon_single_within icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes |
| icon_test load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes |
| load_all_protein_coding_symbols load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes writeGMT write_simple_table |
| load_geneset_symbols network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment term_enrichment term_enrichment term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes writeGMT write_simple_table |
| network_overlap plot.term_enrichment plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| plot.term_enrichment 1 plot.term_enrichment_by_subset 1 readGMT 1 readSIF 1 resource_reduce 1 show_active_genesets_hist 1 summary.term_enrichment 1 summary.term_enrichment 1 term_enrichment 1 term_enrichment 1 term_enrichment_by_subset 2 vac1.day0vs31.de.genes 2 vac2.day0vs31.de.genes 2 vac2.day0vs56.de.genes 2 vac2.day0vs56.de.genes 2 vac2.day0vs56.de.genes 2 vac2.day0vs56.de.genes 3 vac2.day0vs56.de.genes 4 vac2.day0vs56.de.genes 5 vac2.day0vs56.day0vs56.day0vs56.day0vs56.day0vs56.day0vs56.day0vs56.day0vs56.day0v |
| plot.term_enrichment_by_subset readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes |
| readGMT readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| readSIF resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| resource_reduce show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| show_active_genesets_hist summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| summary.term_enrichment summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes |
| summary.term_enrichment_by_subset term_enrichment term_enrichment_by_subset vac1.day0vs31.de.genes vac1.day0vs56.de.genes vac2.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes writeGMT write_simple_table |
| term_enrichment |
| term_enrichment_by_subset vac1.day0vs31.de.genes vac1.day0vs56.de.genes vac2.day0vs31.de.genes vac2.day0vs56.de.genes vac2.day0vs56.de.genes writeGMT write_simple_table |
| vac1.day0vs31.de.genes 2 vac1.day0vs56.de.genes 2 vac2.day0vs31.de.genes 2 vac2.day0vs56.de.genes 2 writeGMT 2 write_simple_table 2 |
| vac1.day0vs56.de.genes2vac2.day0vs31.de.genes2vac2.day0vs56.de.genes2writeGMT2write_simple_table2 |
| vac2.day0vs31.de.genes2vac2.day0vs56.de.genes2writeGMT2write_simple_table2 |
| vac2.day0vs56.de.genes2writeGMT2write_simple_table2 |
| writeGMT |
| write_simple_table |
| |
| In Jan. |
| |
| Index |
| as.graph as.graph |

Description

wrapper to convert a data.frame from RITAN an igraph graph object

Usage

```
as.graph(mat, p1 = 1, p2 = 3, ...)
```

| mat | matrix or data frame describing a network |
|-----|--|
| p1 | [1] column of first interactor |
| p2 | [3] column of second interactor |
| | further options passed on to igraph::graph() |

check_any_net_input 3

Value

igraph object

Examples

```
## Not run:
G <- as.graph(network_list$PID)
## End(Not run)</pre>
```

```
check_any_net_input check_any_net_input
```

Description

A Quality Control function. This function applies check_net_input() to all available resources (default).

Usage

```
check_any_net_input(set, resources = names(network_list))
```

Arguments

set An input list of genes to check against references.

resources The collection of network resources to check within.

Value

Logical vector indicating if the genes in "set" are within ANY of the resources.

```
#' ## Check if genes in myGeneSet are annotated by any resource in "network_list" (default).
library(RITANdata)
myGeneSet <- c('BRCA1', 'RAD51C', 'VAV1', 'HRAS', 'ABCC1', 'CYP1B1', 'CYP3A5')
yorn <- check_any_net_input( myGeneSet )
print(yorn)</pre>
```

4 check_net_input

check_net_input check_net_input

Description

A Quality Control function. This function will compare an input list of genes to a network reference and report if each member of the input is present in the resource.

Usage

```
check_net_input(
   set,
   ref,
   check4similar = FALSE,
   entity1name = "p1",
   entity2name = "p1"
)
```

Arguments

set An input list of genes to check against a reference.

ref A reference of network data. See readSIF().

check4similar Logical flag. If TRUE, a case-insensitive grep will be used for name matching.

For genes in families with many related members (e.g. ABC*, FAM*, etc.), this will not be ideal. We intend this option as a QC screening method to identify if

case, punctuaiton, etc is causing fewer than expected matches.

entity1name The column name in "ref" of the first entity. Default = "p1."

entity2name The column name in "ref" of the second entity. Default = "p2."

Value

Character vector of "yes/no" indicating "within-ref/not"

```
## Return a "yes/no" vector indicating if each gene in myGeneSet is annotated with any term in GO
## If no match, this function can attempt to suggest closest matches (check4similar = TRUE)
library(RITANdata)
myGeneSet <- c('BRCA1', 'RAD51C', 'VAV1', 'HRAS', 'ABCC1', 'CYP1B1', 'CYP3A5')
yorn <- check_net_input( myGeneSet, network_list[["CCSB"]] )
print(yorn)

yorn <- check_net_input( myGeneSet, network_list[["PID"]] )
print(yorn)

## See check_any_net_input() for efficiently checking across all resources.</pre>
```

cov_undirected 5

| nodes tists from two networks | cov_undirected | cov_undirected function to show the un-directed coverabe between two nodes lists from two networks |
|-------------------------------|----------------|--|
|-------------------------------|----------------|--|

Description

cov_undirected function to show the un-directed coverabe between two nodes lists from two networks

Usage

```
cov_undirected(this_nodes1, this_nodes2, this_net1, this_net2)
```

Arguments

this_nodes1 list of nodes for first network
this_nodes2 list of nodes for second network

this_net1 the first network
this_net2 the second network

enrichment_symbols enrichment_symbols

Description

This function is called by term_enrichment() and term_enrichment_by_subset(). The user may call it directly, but we suggest using term_enrichment(). The function uses the resources currently loaded into the active_genesets vector. See load_geneset_symbols().

Usage

```
enrichment_symbols(geneset, term = NULL, all_symbols = NA, ...)
```

| geneset | vector of gene symbols to be evaluated |
|-------------|--|
| term | a list containing specific gene set term(s) and their corresponding gene symbols contained in one of the annotation resources, default is all gene set terms in the GO, ReactomePathways, KEGG_filtered_canonical_pathways, and MSigDB_Hallmarks libraries |
| all_symbols | gene symbols to be evaluated, identified by gene symbol name. Default is all protein coding genes. This parameter should be manipulated to include only the gene symbols that pertain to the user's analysis. |
| | additional arguments are not used |

6 geneset_overlap

Details

Outputs a data frame containing the gene set name, a hypergeometric-test p value, the number of genes from the input gene list that occur in the gene set, the number of genes in the gene set, the gene symbols for the genes in the input gene list, and the q value.

Value

results matrix of input gene list compared to active gene sets. Q value is calculated using entire group of active gene sets.

Examples

```
require(RITANdata)
myGeneSet <- c('BRCA1', 'RAD51C', 'VAV1', 'HRAS', 'ABCC1', 'CYP1B1', 'CYP3A5')</pre>
## Not run:
## We suggest using term_enrichment() instead. E.g.:
e <- term_enrichment(myGeneSet, 'GO')</pre>
## End(Not run)
## But, you may use enrichment_symbols() directly for an individual term:
load_geneset_symbols('GO')
e <- enrichment_symbols(myGeneSet, 'DNA_repair', all_symbols = cached_coding_genes)
print(e)
## Not run:
## Gene set enrichment using intersection of gene symbols
    provided in geneset parameter and all protein coding genes.
enrichment_symbols(geneset = vac1.day0vs31.de.genes)
## choose which terms to evaluate
t <- active_genesets[1:5]
## Test enrichment of that set of terms
enrichment_symbols(geneset = vac1.day@vs31.de.genes, term = t)
## End(Not run)
```

geneset_overlap

geneset_overlap

Description

Return assymetric matrix of the fraction of genes shared between sets. E.G. The fraction of the first set that is "covered" by or "overlaps" the second set.

Usage

```
geneset_overlap(s1, s2 = s1, s.size = unlist(lapply(s1, length)))
```

icon_single_within 7

Arguments

| s1 | The first geneset |
|--------|--|
| s2 | the second geneset |
| s.size | Denominator used in each comparison. The default is to determint the lengths of elements in "s1" |

Value

results matrix of input gene list compared to active gene sets. Q value is calculated using entire group of active gene sets.

Examples

```
require(RITANdata)  r \leftarrow geneset\_overlap(geneset\_list$MSigDB\_Hallmarks, geneset\_list$NetPath\_Gene\_regulation) \\ heatmap(r, col = rev(gray(seq(0,1,length.out = 15))))) \\ summary(c(r))
```

icon_single_within

icon_single_within interconnectivity score within a network

Description

icon_single_within interconnectivity score within a network

Usage

```
icon_single_within(nodes = NULL, net = NULL, s = 10, verbose = TRUE)
```

| nodes | the node labels to use |
|---------|--|
| net | the network to use |
| s | [10] the number of repeated random draws to make |
| verbose | [TRUE] if more verbose output should be shown |

8 icon_test

Description

"icon" is an abbreviation for the "interconnectivity" of a network or graph.

Usage

```
icon_test(nodes1 = NULL, nodes2 = NULL, s = 100, verbose = TRUE, ...)
```

Arguments

| nodes1 | [NULL] the first network. See network_overlap(). |
|---------|---|
| nodes2 | [NULL] the second network. See network_overlap(). |
| S | [100] the number of random permutations to make. |
| verbose | [TRUE] Extent of text shown in the console. |
| | Additional argumetns are passed on to the specific test performed |

Details

This function handles different inputs and directs them to the appropriate "icon" testing method. Depending on the values given to "nodes1" and "nodes2," a different specific test is performed.

Note that the specific functions called make use of the "param" attribute of each input. These parameters are populated by network_overlap() so that the permutation reflects the exact procedure that was done to generate "nodes1" and/or "nodes2."

Value

metrics and significance of the network overlap

```
## Not run:
icon_test( nodes1=n, s=10)
## End(Not run)
```

```
load\_all\_protein\_coding\_symbols \\ load\_all\_protein\_coding\_symbols
```

Description

The character array returned is, by default, all human protein coding gene symbols. This variable defines the "universe of possible genes" for use in enrichment. Users should load a different "universe" or filter this one down to the most appropriate setting for their current study. For example, if running RNA-Seq, genes are in the universie if they are detected in any sample.

Usage

```
load_all_protein_coding_symbols()
```

Value

A unique list of gene symbols for protein coding genes according to EnsDb.Hsapiens.v86

```
load_geneset_symbols load_geneset_symbols
```

Description

For most applications, this function is used internally by term_enrichment(). Users may call this function directly in some cases to force FDR adjustment to be across multiple resources. See Vignette for more details.

Usage

```
load_geneset_symbols(gmt = NA, gmt_dir = "", verbose = TRUE)
```

| gmt | Either 1) name of pre-loaded resource (i.e. names(geneset_list)) or 2) gmt file containing annotation resources for enrichment annotation |
|---------|---|
| gmt_dir | location of gmt file named in gmt parameter |
| verbose | print results to screen |

10 network_overlap

Details

load_geneset_symbols allows the user to specify an annotation resource (e.g. Gene Ontology terms) to use in enrichment analysis. The expectation is that the annotation resource contains of at least one set of genes in the form of a list. The RITAN package comes with 15 pre-loaded annotation resources. The default active annotation resources are GO, ReactomePathways, KEGG_filtered_canonical_pathways, and MSigDB_Hallmarks.

The result of calling this function is to set the variable "active_genesets" which will be used by further functions.

Value

R list object named active_genesets

Examples

```
## Load generic GO-slim terms
require(RITANdata)
load_geneset_symbols("GO_slim_generic")
print(length(active_genesets))
print(head(active_genesets[[1]]))
## Not run:
## load the default set of resources into "active_genesets"
load_geneset_symbols()
## Use only the Reactome Pathways annotation resource.
load_geneset_symbols(gmt="ReactomePathways")
## Suppresses output message describing the annotation resource and size.
load_geneset_symbols(gmt="ReactomePathways", verbose=FALSE)
## To list the available resources within RITAN:
print(names(geneset_list))
## You can also load your own data
load_geneset_symbols(gmt="myFile.gmt")
## End(Not run)
```

network_overlap

network_overlap

Description

network_overlap

network_overlap 11

Usage

```
network_overlap(
  gene_list = NA,
  resources = c("PID", "TFe", "dPPI", "CCSB", "STRING"),
  minStringScore = 700,
  minHumanNetScore = 0.4,
  minScore = 0,
  verbose = TRUE,
  dedup = TRUE,
  directed_net = FALSE,
  include_neighbors = FALSE,
  STRING_cache_directory = NA,
  STRING_species = 9606,
  STRING_version = "10"
)
```

Arguments

gene_list A list of genes to use. The function will identify edges across resources for or

among these genes; identify the induced subnetwork around the gene_list.

resources Name of network resource(s) to use.

minStringScore If STRING is among the resources, only edges of at least the indicated score

will be included.

minHumanNetScore

If HumanNet is among the resources, only edges of at least the indicated score

will be included.

minScore Same as above, but used for any other networks where "score" is provided

verbose If TRUE (default), the function will update the user on what it is doing and how

many edges are identified for each resource.

dedup If TRUE (Default = TRUE), remove edges reported by multiple resources. The

edge type will be a semi-colon delimited list of the resources that had reported

the interaction.

directed_net Logical indicating if the network resources should be interpreted as directed.

include_neighbors

Logical to include 1st neighbors of "gene_list" (genes not in gene_list, but di-

rectly connected to them) in the induced subnetwork.

STRING_cache_directory

A directry where STRING data files are cached to speed up subsequent queries; no need to re-download. If NA (the default), caches STRING data in your Rpackages directory. If "", uses a temporary directory that is cleared when the

R-session closes.

STRING_species Sepcies taxon ID (number) to use in searching STRING data. (Default = 9606)

STRING_version Version of the STRING database (Default = "10")

Value

Data table describing the induced subnetwork for "gene_list" across the requested resources.

12 plot.term_enrichment

Examples

```
## Get interactions among a list of genes from the PID: Pathway Interaction Database
require(RITANdata)
myGeneSet <- c('BRCA1','RAD51C','VAV1','HRAS','ABCC1','CYP1B1','CYP3A5')
sif <- network_overlap( myGeneSet, resources = 'PID')
print(sif)

## Not run:
## Get the PPI network induced by genes within myGeneSet
## Use 4 seperate resources, but trim STRING to only include more confident interactions
sif <- network_overlap( myGeneSet, c('dPPI','PID','CCSB','STRING'), minStringScore = 500 )
## End(Not run)

plot.term_enrichment plot.term_enrichment</pre>
```

Description

plot.term_enrichment

Usage

```
## S3 method for class 'term_enrichment' plot(x = NA, min_q = 0.05, max_terms = 25, extend_mar = c(0, 10, 0, 0), ...)
```

Arguments

| X | data frame returned by term_enrichment |
|------------|--|
| min_q | Only q-values more significant than this threshold will be plotted. Default = 0.05 . |
| max_terms | Up to max_terms will be plotted. Default = 25. |
| extend_mar | Term names can be long. We attempt to keep them readable by extending the left-hand-side margins automatically. Default = $c(0,10,0,0)$ added to par()\$mar. |
| | Additional arguments are passed on to plot() |

Value

silent return from plot

```
require(RITANdata)
e <- term_enrichment(vac1.day0vs31.de.genes, resources = 'GO_slim_generic')
plot(e, min_q = .1)</pre>
```

Description

```
plot.term_enrichment_by_subset
```

Usage

```
## S3 method for class 'term_enrichment_by_subset'
plot(
  show_values = TRUE,
  annotation_matrix = NA,
  low = "white",
  high = "#2166AC",
  return_ggplot_object = FALSE,
  label_size_x = 16,
  label_angle_x = -30,
  label_size_y = 9,
  wrap_y_labels = 20,
  grid_line_color = "white",
 mid = 0,
  cap = NA,
 annotation_palates = c("Reds", "Greens", "Purples", "Greys", "BuPu", "RdPu", "BrBG",
    "PiYG", "Spectral"),
  annotation_legend_x = -0.3,
  trim_resource_names = TRUE,
)
```

```
data frame returned by term_enrichment_by_subset
Х
show_values
                  True or False, plot values on the heatmap
annotation_matrix
                  a matrix() of group-levle characteristics - same number of columns as "m"
                  color for low end of range
low
high
                  color for high end of range
return_ggplot_object
                  logical flag (default FALSE) that if TRUE, the ggplot object for the plot is re-
                  size of text for x label. Default lable_size_x=16
label_size_x
                  angle for text for x label. Default is -30 degrees
label_angle_x
```

14 readGMT

```
label_size_y
                  size of text for y label. Default label_size_y=9
wrap_y_labels
                  Number of characters to wrap row labels
grid_line_color
                  color o grid lines between cells. Default is white.
mid
                  sets lower threshold for color scale
cap
                  Clip numeric values to this maximum threshold
annotation_palates
                  Color palates (RColorBrewer) used for each row of the annotation matrix
annotation_legend_x
                  offset for placing the legend
trim_resource_names
                  [TRUE] remove any text in rownames preceding a period characte. This con-
                  vension is usually used in RITAN to prepend the resource name to the term
                  name, which may not be needed in plotting.
                  further areguments are not used at this time. If the user wants to modify the plot,
                  use return_ggplot_object = TRUE.
```

Value

silent return, unless return_ggplot_object==TRUE. Then, the ggplot object for the plot is returned.

Examples

```
## Create list of gene sets to evaluate.
## This example is from a vaccine study where we pre-generated differentially expressed genes.
## This object will be passed to the groups parameter.
require(RITANdata)
vac1.de.genes <- list(vac1.day0vs31.de.genes, vac1.day0vs56.de.genes)
names(vac1.de.genes) <- c("Day0vs31", "Day0vs56")
print(str(vac1.de.genes))
## Not run:
## Run term_enrichment_by_subset on the two results.
## This function usually takes a few seconds to a minute to run.
m <- term_enrichment_by_subset(groups = vac1.de.genes, q_value_threshold = .9)
summary(m)
plot( m, label_size_y = 4, show_values = FALSE )
## End(Not run)</pre>
```

readGMT

readGMT

Description

Created for simplification of reading .gmt files into RITAN.

readSIF 15

Usage

```
readGMT(f = NA)
```

Arguments

f

GMT file name. Please provide a full path if the file is not in the current working directory.

Value

A list() where the name of each entry is the term (first column of GMT file) and the value is a chr array of genes associated with the term.

Examples

readSIF

readSIF

Description

This function reads a data table into R; the data table describes network interactions. It is named for the Simple Interaction Format (SIF), but can read any data table if the users identifies which columns contain the pertinent data (see below).

Usage

```
readSIF(
  file = NA,
  header = FALSE,
  sep = "\t",
  as.is = TRUE,
```

16 readSIF

```
p1 = 1,
p2 = 2,
et = 3,
score = NA,
...
```

Arguments

| file | location of file |
|--------|--|
| header | indicator of presense of header on file |
| sep | file delimiter - used by read.table() |
| as.is | logical (default TRUE) |
| p1 | Column number for the 1st entity. Default = 1. |
| p2 | Column number for the 2nd entity. Default = 2 . |
| et | Column number for the edge type. Default = 3. Optionally, it may be a string label to be used as the edge type for all interactions from the input file. |
| score | Column number for edge scores or weights. Default = NA (no score read). |
| | Other options to read.table(). |

Details

The SIF file format is a 3-column format, with an optional 4th column: <entity-1><tab><edge-type><tab><entity-2><tab><score>

Entities may be genes, proteins, metabolites, etc. The edge type typically conveys the type of relationship that exists between the two entities, such as physical interaction, phosphorylation, or activation.

Value

Returns a data.frame with 3 (or 4) columns of data.

resource_reduce 17

| resource_reduce | resource_reduce Merge terms across resources to reduce the number of redundant and semi-redundant terms |
|-----------------|---|
| | · |

Description

resource_reduce Merge terms across resources to reduce the number of redundant and semi-redundant terms

Usage

```
resource_reduce(genesets = NULL, min_overlap = 0.8, verbose = TRUE)
```

Arguments

genesets the input genesets to consider. May be from one or multiple resources.

min_overlap terms that share at least this fraction of genes will be merged

verbose if TRUE, print status and summary output

Value

the list of terms, after merging to reduce redundant and semi-redundant terms

Examples

Description

function to plot distribution of size of active_genesets object

Usage

```
show_active_genesets_hist(nbins = 50, ...)
```

| nbins | Number of bins to include in histogram |
|-------|---|
| | further argumants are passed on to plot() |

Value

NULL. The plot is shown.

Examples

```
require(RITANdata)
load_geneset_symbols('GO_slim_generic')
show_active_genesets_hist()

## Not run:
## Show the distribution of geneset sizes for the default set of geneset resources
load_geneset_symbols()
show_active_genesets_hist()

## Show the distribution of geneset sizes for a specific resource
load_geneset_symbols(gmt="ReactomePathways")
show_active_genesets_hist()

## End(Not run)

summary.term_enrichment

summary.term_enrichment
```

Description

summary.term_enrichment

Usage

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

Arguments

object data frame returned by term_enrichment()
... Further arguments are passed on to head()

Value

the data.frame of top enrichment results

```
require(RITANdata)
e <- term_enrichment( vac1.day0vs31.de.genes, "MSigDB_Hallmarks" )
summary(e, n=3)</pre>
```

```
summary.term\_enrichment\_by\_subset \\ summary.term\_enrichment\_by\_subset
```

Description

```
summary.term_enrichment_by_subset
```

Usage

```
## S3 method for class 'term_enrichment_by_subset'
summary(object, verbose = TRUE, ...)
```

Arguments

object data frame returned by term_enrichment_by_subset()
verbose if TRUE (default), print a header describing the data type
... Further arguments are passed on to head()

Value

the data.frame of top enrichment results

Examples

```
require(RITANdata)
vac1.de.genes <- list(vac1.day0vs31.de.genes, vac1.day0vs56.de.genes)
names(vac1.de.genes) <- c("Day0vs31", "Day0vs56")
e <- term_enrichment_by_subset(vac1.de.genes, "MSigDB_Hallmarks", q_value_threshold = 0.1 )
summary(e)</pre>
```

term_enrichment term_enrichment

Description

term_enrichment evaluates the input gene list for enrichment within each of the annotation resources. This differs from the enrichment_symbols function which evaluates the gene list for enrichment against all of the annotation resources grouped together.

20 term_enrichment

Usage

```
term_enrichment(
  geneset,
  resources = resources.default,
  report_resources_separately = FALSE,
  verbose = TRUE,
  all_symbols = NA,
  filter_to_intersection = FALSE,
  ...
)
```

Arguments

geneset vector of gene symbols to be evaluated

resources list containing the reference gene sets to test for enrichment

report_resources_separately

logical (default FALSE) flag to report enrichments seperately for each requested resource, or to combine them and produce FDR adjustment across the combined

set

verbose print the top results for each annotation resource

all_symbols the background/global set of gene symbols (study dependent; we provide all

protien coding genes as a default)

filter_to_intersection

[FALSE] should the background and foreground genesets be subsetted to one

another?

... further arguments are passed on to enrichment_symbols()

Value

results matrix of input gene list compared to active gene sets. Q value is calculated within each of the active gene sets.

```
## Check if there is enrichment for any "Hallmark" functions within a input set of genes
require(RITANdata)
myGeneSet <- c('BRCA1', 'RAD51C', 'VAV1', 'HRAS', 'ABCC1', 'CYP1B1', 'CYP3A5')
e <- term_enrichment(myGeneSet, "MSigDB_Hallmarks")
print( e[1:2, -6] )

## Not run:
term_enrichment(geneset = vac1.day0vs31.de.genes)
term_enrichment(geneset = vac1.day0vs31.de.genes, resources = "MSigDB_Hallmarks")
vac1.day0v31.enrichment <- term_enrichment(geneset = vac1.day0vs31.de.genes, verbose = FALSE)
## End(Not run)</pre>
```

Description

Run enrichment simultaneously across a group of prioritized gene lists. For example, in a time course dataset, one may have a different list of genes that are differentially expressed at each time point. This function facilitates rapid evaluation of term enrichment across time point comparisons. Alternatively, one may have a different list of differentially expressed genes by drug treatment, environmental condition, ect.

Usage

```
term_enrichment_by_subset(
  groups = NA,
  resources = resources.default,
  q_value_threshold = 0.01,
  verbose = TRUE,
  display_type = "q",
  phred = TRUE,
  ...
)
```

Arguments

groups A list() of genes for enrichment. Each entry in the list() is an input set of genes.

Enrichment is performed for each of these entries.

resources character vector for which resources to use in enrichment

q_value_threshold

minimum q-value (FDR adjusted p-value) in any group for the term to be in-

cluded in results

verbose print additional status updates on what the function is doing

display_type Flag for which data type will be returned. One of "q" (default) for q-values, "p"

for unadjusted p-values, or "n" for the number of genes overlapping the term.

phred Logical flag (default TRUE) to return the -log10 of p/q values

... Further arguments are passed on to enrichment_symbols()

Value

Returns a term-by-study matrix of enrichment values (value determined by "display_type")

Examples

```
## Create list of gene sets to evaluate.
## This example is from a vaccine study where we pre-generated differentially expressed genes.
## This object will be passed to the groups parameter.
require(RITANdata)
vac1.de.genes <- list(vac1.day0vs31.de.genes, vac1.day0vs56.de.genes)
names(vac1.de.genes) <- c("Day0vs31", "Day0vs56")
print(str(vac1.de.genes))

## Not run:
## Run term_enrichment_by_subset on the two results.
## This function usually takes a few seconds to a minute to run.
m <- term_enrichment_by_subset(groups = vac1.de.genes, q_value_threshold = .9)
summary(m)
plot( m, label_size_y = 4, show_values = FALSE )

## End(Not run)</pre>
```

vac1.day0vs31.de.genes

This dataset is included as an example in the package:

Description

This dataset is included as an example in the package:

Usage

```
vac1.day0vs31.de.genes
```

Format

An object of class character of length 669.

Value

differentially expressed genes at 31 days post-vaccination with vaccine1

References

```
https://www.ncbi.nlm.nih.gov/pubmed/26755593
```

vac1.day0vs56.de.genes 23

Examples

```
## Not run:
  #data("vac1.day0vs31.de.genes")
  te <- term_enrichment(geneset = vac1.day0vs31.de.genes)
## End(Not run)</pre>
```

```
vac1.day0vs56.de.genes
```

This dataset is included as an example in the package:

Description

This dataset is included as an example in the package:

Usage

```
vac1.day0vs56.de.genes
```

Format

An object of class character of length 471.

Value

differentially expressed genes at 56 days post-vaccination with vaccine1

References

```
https://www.ncbi.nlm.nih.gov/pubmed/26755593
```

```
## Not run:
  #data("vac1.day0vs56.de.genes")
  te <- term_enrichment(geneset = vac1.day0vs56.de.genes)
## End(Not run)</pre>
```

```
vac2.day0vs31.de.genes
```

This dataset is included as an example in the package:

Description

This dataset is included as an example in the package:

Usage

```
vac2.day0vs31.de.genes
```

Format

An object of class character of length 522.

Value

differentially expressed genes at 31 days post-vaccination with vaccine2

References

```
https://www.ncbi.nlm.nih.gov/pubmed/26755593
```

Examples

```
## Not run:
  #data("vac2.day0vs31.de.genes")
  te <- term_enrichment(geneset = vac2.day0vs31.de.genes)
## End(Not run)</pre>
```

```
vac2.day0vs56.de.genes
```

This dataset is included as an example in the package:

Description

This dataset is included as an example in the package:

Usage

```
vac2.day0vs56.de.genes
```

writeGMT 25

Format

An object of class character of length 660.

Value

differentially expressed genes at 56 days post-vaccination with vaccine2

References

```
https://www.ncbi.nlm.nih.gov/pubmed/26755593
```

Examples

```
## Not run:
  #data("vac2.day0vs56.de.genes")
  te <- term_enrichment(geneset = vac2.day0vs56.de.genes)
## End(Not run)</pre>
```

writeGMT

writeGMT

Description

Created for future use and simplification of writing .gmt files from the package.

Usage

```
writeGMT(s, file = NA, link = rep("", length(s)))
```

Arguments

s list of gene sets in current R session. Each entry will become a row in the GMT

file file name to write to

link default is "". This is the second column of a GMT file and is usually a hyperlink

or note about the origin of the term

Value

Nothing is returned. A file is written.

26 write_simple_table

Examples

write_simple_table

write_simple_table

Description

This is a simple wrapper around "write.table" that writes a tab-delimited table with column names, no quoting, and no row names.

Usage

```
write_simple_table(d = NULL, f = NULL, ...)
```

Arguments

d R data object f file path

... further options passed on to write.table

Value

invisible (nothing is returned)

```
## Not run:
simple wrapper around write.table for writing a tab-delimieted, no row names, tab-seperated file
## End(Not run)
```

Index

```
* datasets
    vac1.day0vs31.de.genes, 22
    vac1.day0vs56.de.genes, 23
    vac2.day0vs31.de.genes, 24
    vac2.day0vs56.de.genes, 24
as.graph, 2
check_any_net_input, 3
check_net_input, 4
cov_undirected, 5
\verb"enrichment_symbols", 5
geneset_overlap, 6
icon_single_within, 7
icon_test, 8
load_all_protein_coding_symbols, 9
load_geneset_symbols, 9
network_overlap, 10
plot.term_enrichment, 12
plot.term_enrichment_by_subset, 13
readGMT, 14
readSIF, 15
resource_reduce, 17
show_active_genesets_hist, 17
summary.term_enrichment, 18
\verb|summary.term_enrichment_by_subset|, 19|
term_enrichment, 19
term_enrichment_by_subset, 21
vac1.day0vs31.de.genes, 22
vac1.day0vs56.de.genes, 23
vac2.day0vs31.de.genes, 24
vac2.day0vs56.de.genes, 24
write_simple_table, 26
writeGMT, 25
```