Package 'hipathia'

October 16, 2022

Title HiPathia: High-throughput Pathway Analysis

Version 2.12.0

signaling pathways from transcriptomic data. The method is based on an iterative algorithm which is able to compute the signal intensity passing through the nodes of a network by taking into account the level of expression of each gene and the intensity of the signal arriving to it. It also provides a new approach to functional analysis allowing to compute the signal arriving to the functions annotated to each pathway. **Depends** R (>= 3.6), igraph (>= 1.0.1), AnnotationHub(>= 2.6.5), MultiAssayExperiment(>= 1.4.9), SummarizedExperiment(>= 1.8.1) License GPL-2 **Encoding UTF-8** LazyData true **Imports** coin, stats, limma, grDevices, utils, graphics, preprocessCore, servr, DelayedArray, matrixStats, methods, S4Vectors RoxygenNote 7.0.0 Suggests BiocStyle, knitr, rmarkdown, testthat VignetteBuilder knitr biocViews Pathways, GraphAndNetwork, GeneExpression, GeneSignaling, GO git_url https://git.bioconductor.org/packages/hipathia git_branch RELEASE_3_15 git_last_commit db2d24b git_last_commit_date 2022-04-26 **Date/Publication** 2022-10-16 **Author** Marta R. Hidalgo [aut, cre], José Carbonell-Caballero [ctb], Francisco Salavert [ctb], Alicia Amadoz [ctb],

Description Hipathia is a method for the computation of signal transduction along

Çankut Cubuk [ctb], Joaquin Dopazo [ctb]

Maintainer Marta R. Hidalgo <marta.hidalgo@outlook.es>

R topics documented:

annotate_paths	3
brca	4
brca_data	4
brca_design	5
comp	6
create_report	6
do_pca	7
do_wilcoxon	8
exp_data	9
<i>c</i>	10
get_highest_sig_ancestor	11
get_nodes_data	11
6 = =	12
get_paths_data	13
get_pathways_annotations	14
get_pathways_list	15
get_pathways_summary	15
get_pathway_functions	16
get_path_names	17
go_vals	18
heatmap_plot	18
hhead	20
hipathia	21
	22
	22
load_annofuns	23
load_annots	23
load_entrez_hgnc	24
load_gobp_frame	24
load_gobp_net	25
load_mgi	25
	26
load_pseudo_mgi	27
	27
	28
multiple_pca_plot	28
node_color	29
	31
	32
	34
_1	34

annotate_paths 3

	pathway_comparison_plot	35
	path_vals	37
	pca_plot	37
	quantify_terms	39
	results	40
	save_results	40
	top_pathways	41
	translate_data	41
	translate_matrix	42
	visualize_report	43
Index		44

annotate_paths

Annotates functions to pathways

Description

Annotates functions from a database to each pathway

Usage

```
annotate_paths(metaginfo, dbannot)
```

Arguments

metaginfo Pathways object

dbannot Either a string indicating which precomputed annotation to use ("uniprot" for

Uniprot Keywords or "GO" for Gene Ontology terms), or a dataframe with the annotation of the genes to the functions. First column are gene symbols, second

column the functions.

Value

Object of annotations from pathways to functions

```
\label{eq:condition} $$\#@ examples \#pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320", \#"hsa04012")) $$\#annotate_paths(pathways, "GO")$
```

#@export

4 brca_data

brca

BRCA gene expression dataset as SummarizedExperiment

Description

A dataset containing a matrix with the Gene expression of 40 samples from the BRCA-US project from The Cancer Genome Atlas (TCGA), and their experimental design, containing 20 "Tumor" samples 20 "Normal" samples.

Usage

data(brca)

Format

SummarizedExperiment. The assay is a matrix with 40 columns and 18638 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples. The colData() is a data.frame with 1 column and 40 rows, including the experimental design of the 40 samples from the BRCA-US project from TCGA. Field group is the type of sample, either "Tumor" or "Normal".

Details

The gene expression matrix includes 40 samples. The data has been log-transformed and normalized with TMM.

Value

SummarizedExperiment including a matrix with 40 columns and 18638 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples.

Source

https://cancergenome.nih.gov/

brca_data

BRCA gene expression dataset

Description

Gene expression of 40 samples from the BRCA-US project from The Cancer Genome Atlas (TCGA).

Usage

data(brca_data)

brca_design 5

Format

Matrix with 40 columns and 18638 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples.

Details

Gene expression matrix with 40 samples taken from the BRCA-US project from The Cancer Genome Atlas (TCGA). The data has been log-transformed and normalized with TMM.

Value

Matrix with 40 columns and 18638 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples.

Source

```
https://cancergenome.nih.gov/
```

brca_design

BRCA experimental design

Description

Experimental design of the gene expression matrix brca_data with 40 samples taken from the BRCA-US project from The Cancer Genome Atlas (TCGA). 20 samples are "Tumor" samples and 20 samples are "Normal" samples.

Usage

```
data(brca_design)
```

Format

Dataframe with 1 column and 40 rows, including the experimental design of the 40 samples from the BRCA-US project from TCGA. Field group is the type of sample, either "Tumor" or "Normal".

Value

Dataframe with 1 column and 40 rows, including the experimental design of the 40 samples from the BRCA-US project from TCGA. Field group is the type of sample, either "Tumor" or "Normal".

Source

```
https://cancergenome.nih.gov/
```

6 create_report

comp

Wilcoxon comparison of pathways object

Description

```
Comparison object returned by hipathia::do_wilcoxon function, after calling comp <- do_wilcoxon(path_vals, sample_group, g1 = "Tumor", g2 = "Normal") path_names <- get_path_names(pathways, rownames(comp)) comp <- cbind(path_names, comp)
```

Usage

```
data(comp)
```

Format

Table with 1868 rows and 5 columns

Value

Pathway comparison result

create_report

Create visualization HTML

Description

Saves the results of a Wilcoxon comparison for the Hipathia pathway values into a folder, and creates a HTML from which to visualize the results on top of the pathways. The results are stored into the specified folder. If this folder does not exist, it will be created. The parent folder must exist.

Usage

```
create_report(
  comp,
  metaginfo,
  output_folder = NULL,
  path = NULL,
  node_colors = NULL,
  group_by = "pathway",
  conf = 0.05,
  verbose = FALSE
)
```

do_pca 7

Arguments

comp Comparison object as given by the do_wilcoxon function
metaginfo Pathways object as returned by the load_pathways function

output_folder Name of the folder in which the report will be stored.

path Absolute path to the parent directory in which 'output_folder' will be saved. If

it is not provided, it will be created in a temp folder.

node_colors List of colors with which to paint the nodes of the pathways, as returned by the

node_color_per_de function. Default is white.

group_by How to group the subpathways to be visualized. By default they are grouped

by the pathway to which they belong. Available groupings include "uniprot", to group subpathways by their annotated Uniprot functions, "GO", to group subpathways by their annotated GO terms, and "genes", to group subpathways by

the genes they include. Default is set to "pathway".

conf Level of significance. By default 0.05.

verbose Boolean, whether to show details about the results of the execution

Value

Saves the results and creates a report to visualize them through a server in the specified output_folder. Returns the folder where the report has been stored.

Examples

```
data(comp)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
report <- create_report(comp, pathways, "save_results")

## Not run:
data(results)
data(brca)
sample_group <- colData(brca)[,1]
colors_de <- node_color_per_de(results, pathways,
sample_group, "Tumor", "Normal")
report_colors <- create_report(comp, pathways, "save_results",
node_colors = colors_de)

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

do_pca

Performs a Principal Components Analysis

Description

Performs a Principal Components Analysis

8 do_wilcoxon

Usage

```
do_pca(data, sel_assay = 1, cor = FALSE)
```

Arguments

SummarizedExperiment or matrix of values to be analyzed. Samples must be represented in the columns.

Sel_assay

Character or integer, indicating the assay to be normalized in the Summarized-Experiment. Default is 1.

Cor

A logical value indicating whether the calculation should use the correlation matrix or the covariance matrix. (The correlation matrix can only be used if there are no constant variables.)

Value

do_pca returns a list with class princomp.

Examples

```
data(path_vals)
pca_model <- do_pca(path_vals[seq_len(ncol(path_vals)),])</pre>
```

do_wilcoxon

Apply Wilcoxon test

Description

Performs a Wilcoxon test for the values in sel_vals comparing conditions g1 and g2

Usage

```
do_wilcoxon(
  data,
  group,
  g1,
  g2,
  paired = FALSE,
  adjust = TRUE,
  sel_assay = 1,
  order = FALSE
)
```

exp_data 9

Arguments	
1 LI Sullicitus	

data	Either a SummarizedExperiment object or a matrix, containing the values. Columns represent samples.
group	Either a character indicating the name of the column in colData including the classes to compare, or a character vector with the class to which each sample belongs. Samples must be ordered as in data
g1	String, label of the first group to be compared
g2	String, label of the second group to be compared
paired	Boolean, whether the samples to be compared are paired. If TRUE, function wilcoxsign_test from package coin is used. If FALSE, function wilcox.test from package stats is used.
adjust	Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method
sel_assay	Character or integer, indicating the assay to be normalized in the Summarized-Experiment. Default is 1.
order	Boolean, whether to order the results table by the FDRp.value column. Default is FALSE.

Value

Dataframe with the result of the comparison

Examples

```
data(path_vals)
data(brca_design)
sample_group <- brca_design[colnames(path_vals),"group"]
comp <- do_wilcoxon(path_vals, sample_group, g1 = "Tumor", g2 = "Normal")</pre>
```

exp_data

Normalized BRCA gene expression dataset

Description

Experimental design matrix once expression matrix brca_data has been translated to Entrez geens with translate_matrix and normalized using normalize_data.

Usage

```
data(exp_data)
```

Format

Matrix with 40 columns and 3184 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples.

10 get_go_names

Details

To create the data, the following functions have been called: trans_data <- translate_matrix(brca_data, "hsa") exp_data <- normalize_data(trans_data)

Value

Matrix with 40 columns and 3184 rows. Row names are Entrez IDs and column names are the TCGA identifyers of the samples.

get_go_names

Tranlates GO IDs to GO names

Description

Translates the GO IDs to readable and comprensible names.

Usage

```
get_go_names(names, species, maxchar = NULL)
```

Arguments

names Character vector with the GO IDs to be translated.

species Species of the samples.

maxchar Integer, describes the number of maximum characters to be shown. By default

no filter is applied.

Value

A character vector including the readable names of the GO IDs, in the same order as provided.

```
data(go_vals)
get_go_names(rownames(go_vals), "hsa")
```

```
get_highest_sig_ancestor
```

Get highest common GO ancestor of GO annotations

Description

Get highest common GO ancestor of GO annotations

Usage

```
get_highest_sig_ancestor(
  go_terms,
  go_comp,
  metaginfo,
  unique = TRUE,
  pval = 0.05
)
```

Arguments

go_terms GO terms for which the highest common ancestors are to be looked for.

go_comp Wilcoxon comparison of the matrix of GO values as returned by do_wilcoxon.

metaginfo Pathways object

unique Boolean, whether to return only one highest significant GO ancestor or all of

them. By default, TRUE.

pval P-value cut-off. Default values is set to 0.05.

Value

highest common ancestors

#@export

get_nodes_data Gets the

Gets the object of node activation values

Description

This function returns the object with the levels of activation of each node for each sample. Rows represent the nodes and columns represent the samples. Each cell is the value of activation of a node in a sample.

 $Rownames\ are\ the\ IDs\ of\ the\ nodes\ In\ order\ to\ transform\ IDs\ into\ readable\ names,\ use\ {\tt get_node_names}.$

Effector subpathways are subgraphs of a pathway including all the paths leading to an effector protein. Effector proteins are defined as final nodes in the graph. Each effector protein (final node) in a pathway defines its own effector subpathway as the nodes and edges in a path leading to it.

12 get_node_names

Decomposed subpathways are subgraphs of a pathway including all the paths starting in a receptor protein and ending in an effector protein. Receptor proteins are defined as initial nodes and effector proteins are defined as final nodes in the graph. Each effector subpathway can be decomposed in as many decomposed subpathways as initial nodes it includes.

Usage

```
get_nodes_data(results, matrix = FALSE)
```

Arguments

results Results object as returned by hipathia.

matrix Boolean, if TRUE the function returns a matrix object, if FALSE (as default)

returns a SummarizedExperiment object.

Value

Object, either a SummarizedExperiment or a matrix, with the levels of activation of each decomposed subpathway for each sample.

Examples

```
data(results)
path_vals <- get_paths_data(results)</pre>
```

get_node_names

Tranlates node IDs to node names

Description

Translates the node IDs to readable and comprensible names.

The names of the nodes are encoded as "pathway: name", where "pathway" is the pathway to which the node belongs and "node" is the name of the node. Nodes may include more genes than the one depicted in the name.

Usage

```
get_node_names(metaginfo, names, maxchar = NULL)
```

Arguments

metaginfo Pathways object

names Character vector with the subpathway IDs to be translated

maxchar Integer, describes the number of maximum characters to be shown. By default

no filter is applied.

get_paths_data 13

Value

A character vector including the readable names of the subpathways IDs, in the same order as provided.

Examples

```
data(results)
pathways_list <- c("hsa03320", "hsa04012")
pathways <- load_pathways(species = "hsa", pathways_list)
node_vals <- get_nodes_data(results)
translated_names <- get_node_names(pathways, rownames(node_vals))</pre>
```

get_paths_data

Gets the object of subpathway activation values

Description

This function returns the object with the levels of activation of each subpathway for each sample. Rows represent the subpathways and columns represent the samples. Each cell is the value of activation of a subpathway in a sample.

Rownames are the IDs of the subpathways. In order to transform IDs into readable names, use get_path_names.

Effector subpathways are subgraphs of a pathway including all the paths leading to an effector protein. Effector proteins are defined as final nodes in the graph. Each effector protein (final node) in a pathway defines its own effector subpathway as the nodes and edges in a path leading to it.

Decomposed subpathways are subgraphs of a pathway including all the paths starting in a receptor protein and ending in an effector protein. Receptor proteins are defined as initial nodes and effector proteins are defined as final nodes in the graph. Each effector subpathway can be decomposed in as many decomposed subpathways as initial nodes it includes.

Usage

```
get_paths_data(results, matrix = FALSE)
```

Arguments

results Results object as returned by hipathia.

matrix Boolean, if TRUE the function returns a matrix object, if FALSE (as default)

returns a SummarizedExperiment object.

Value

Object, either a SummarizedExperiment or a matrix, with the levels of activation of each decomposed subpathway for each sample.

Examples

```
data(results)
path_vals <- get_paths_data(results)</pre>
```

```
get_pathways_annotations
```

Get Pathways functional annotations

Description

Get functional annotation of the pathways, either for a particular annotation or a stored one.

Usage

```
get_pathways_annotations(pathway_names, metaginfo, dbannot, collapse = FALSE)
```

Arguments

metaginfo Pathways object

dbannot Either a string indicating which precomputed annotation to use ("uniprot" for

Uniprot Keywords or "GO" for Gene Ontology terms), or a dataframe with the annotation of the genes to the functions. First column are gene symbols, second

column the functions.

collapse Boolean, whether to collapse all functions of the same path in a single character

string.

Value

2-columns matrix with the annotations of each pathway ID in the annotation dbannot.

```
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
pathway_names <- c("P-hsa03320-37", "P-hsa03320-61", "P-hsa03320-46",
    "P-hsa03320-57", "P-hsa03320-64", "P-hsa03320-47", "P-hsa03320-65")
## Not run: get_pathways_annotations(pathway_names, pathways, "GO")
get_pathways_annotations(pathway_names, pathways, "uniprot")</pre>
```

get_pathways_list 15

get_pathways_list

Lists the IDs of the pathways in a pathways object

Description

Lists the IDs of the pathways included in the pathways object metaginfo

Usage

```
get_pathways_list(metaginfo)
```

Arguments

metaginfo

Pathways object

Value

List of the pathway IDs included in the pathways object

Examples

```
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
pathways_list <- get_pathways_list(pathways)</pre>
```

get_pathways_summary

Compute pathway summary

Description

Computes a summary of the results, summarizing the number and proportion of up- and down-regulated subpathways in each pathway.

Usage

```
get_pathways_summary(comp, metaginfo, conf = 0.05)
```

Arguments

comp Comparison data frame as returned by the do_wilcoxon function.

metaginfo Pathways object

conf Level of significance of the comparison for the adjusted p-value. Default is 0.05.

Value

Table with the summarized information for each of the pathways. Rows are the analized pathways. Columns are: * num_total_paths Number of total subpathways in which each pathway is decomposed. * num_significant_paths Number of significant subpathways in the provided comparison. * percent_significant_paths Percentage of significant subpathways from the total number of subpathways in a pathway. * num_up_paths Number of significant up-regulated subpathways in the provided comparison. * percent_up_paths Percentage of significant up-regulated subpathways from the total number of subpathways in a pathway. * num_down_paths Number of significant down-regulated subpathways in the provided comparison. * percent_down_paths Percentage of significant down-regulated subpathways from the total number of subpathways in a pathway.

Examples

```
data(comp)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
get_pathways_summary(comp, pathways)</pre>
```

get_pathway_functions Returns functions related to a pathway

Description

Returns functions related to a pathway

Dotherson object

Usage

```
get_pathway_functions(
  pathigraph,
  dbannot,
  entrez2hgnc,
  use_last_nodes = TRUE,
  unique = TRUE
)
```

Arguments

na+h; ~nanh

patnigrapn	Patnway object
dbannot	Dataframe with the annotation of the genes to the functions. First column are gene symbols, second column the functions.
entrez2hgnc	Relation between Entrez and HGNC genes.
	Boolean, whether to annotate functions to the last nodes of the pathways or not. If FALSE, functions will refer to all the nodes of the pathway.
unique	Boolean, whether to return the first function for each path.

get_path_names 17

Value

List of annotations from pathways to functions

get_path_names

Tranlates path IDs to path names

Description

Translates the subpathway IDs to readable and comprensible names.

For effector subpathways, the names of the subpathways are encoded as "pathway: effector_protein", where "pathway" is the pathway to which the subpathway belongs and "effector_protein" is the name of the last node in the subpathway.

For decomposed subpathways, the names of the subpathways are encoded as "pathway: receptor_protein - effector_protein", where "pathway" is the pathway to which the subpathway belongs, "receptor_protein" is the name of the initial node of the subpathway and "effector_protein" is the name of the last node in the subpathway.

Usage

```
get_path_names(metaginfo, names, maxchar = NULL)
```

Arguments

metaginfo Pathways object

names Character vector with the subpathway IDs to be translated

maxchar Integer, describes the number of maximum characters to be shown. By default

no filter is applied.

Value

A character vector including the readable names of the subpathways IDs, in the same order as provided.

```
data(path_vals)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
translated_names <- get_path_names(pathways, rownames(path_vals))</pre>
```

18 heatmap_plot

go_vals

Gene Ontology matrix of the BRCA gene expression dataset

Description

Matrix of Gene Ontology terms activation values for the BRCA dataset. This matrix is computed from the Results object returned by the hipathia function by means of the quantify_terms function.

Usage

```
data(go_vals)
```

Format

Matrix with 40 columns and 1654 rows. Row names are Gene Ontology terms and column names are the TCGA identifyers of the samples.

Details

```
go_vals <- quantify_terms(results, pathways, "GO")</pre>
```

Value

Matrix with 40 columns and 1654 rows. Row names are Gene Ontology terms and column names are the TCGA identifyers of the samples.

heatmap_plot

Plots subpathways heatmap

Description

Plots a heatmap with the values of the subpathways.

Usage

```
heatmap_plot(
  data,
  group = NULL,
  sel_assay = 1,
  colors = "classic",
  sample_clust = TRUE,
  variable_clust = FALSE,
  labRow = NULL,
  labCol = NULL,
  sample_colors = NULL,
```

heatmap_plot 19

```
scale = TRUE,
save_png = NULL,
legend = TRUE,
legend_xy = "topright",
pch = 15,
main = NULL
)
```

Arguments

data Either a SummarizedExperiment or a matrix with the values to be plotted. Rows

are features and columns are samples.

group Either a character indicating the name of the column in colData including the

classes to plot, or a character vector with the class to which each sample belongs. Samples must be ordered as in data. By default, all samples will be assigned to

the same class.

sel_assay Character or integer, indicating the assay to be normalized in the Summarized-

Experiment. Default is 1.

colors Either a character vector with colors or a key name indicating the color scheme

to be used in the heatmap. If a character vector is provided, it is recommended to provide at least 3 colors. Three different predefined color schemes may be selected by providing a key name. Options are: *classic Blue for lower values, white for medium values, red for higher values. *hipathia Hipathia predefined color scheme: Green for lower values, white for medium values, orange for higher values. *redgreen Green for lower values, black for medium values,

red for higher values. By default classic color scheme is applied.

sample_clust Boolean, whether to cluster samples (columns). By default TRUE.

variable_clust Boolean, whether to cluster variables (rows). By default FALSE. If TRUE, rows

with 0 variance are removed.

labRow, labCol Character vectors with row and column labels to be used. By default row-

names(data) or colnames(data) are used, respectively.

sample_colors Named character vector of colors. The names of the colors must be the classes

in group. Each sample will be assigned the color corresponding to its class, taken from the group vector. By default a color will be assigned automatically

to each class.

scale Boolean, whether to scale each row to the interval [0,1]. Default is TRUE.

save_png Path to the file where the image as PNG will be saved. By default, the image is

not saved.

legend Boolean, whether to display a legend.

legend_xy Position for the legend, in case legend is TRUE.

pch Graphical parameter from par() function.

main Main title of the image

Value

Heatmap of the values of the subpathways

20 hhead

Examples

```
data(brca_design)
data(path_vals)
sample_group <- brca_design[colnames(path_vals),"group"]
heatmap_plot(path_vals, group = sample_group)
heatmap_plot(path_vals, group = "group", colors = "hipathia",
variable_clust = TRUE)</pre>
```

hhead

Head function for SummarizedExperiment, data.frames and matrix objects

Description

Shows the first n rows and the first n columns of a matrix, in case the matrix has more than n+5 rows or columns. Otherwise, it shows all the rows or columns, respectively.

Usage

```
hhead(mat, n = 5, sel_assay = 1)
```

Arguments

mat	Object to be shown
n	Number of rows and columns
sel_assay	Character or integer, indicating the assay to be translated in the SummarizedExperiment. Default is 1.

Value

Matrix with as much as n rows and n columns.

```
mat <- matrix(rnorm(100), ncol = 10)
hhead(mat)
hhead(mat, 3)
hhead(mat, 7)</pre>
```

hipathia 21

	hipathia	Computes the level of activation of the subpathways for each of the samples
--	----------	-----------------------------------------------------------------------------

Description

#@importFrom igraph

Usage

```
hipathia(
  genes_vals,
  metaginfo,
  sel_assay = 1,
  decompose = FALSE,
  maxnum = 100,
  verbose = TRUE,
  tol = 1e-06,
  test = TRUE
)
```

Arguments

genes_vals	A SummarizedExperiment or matrix with the normalized expression values of the genes. Rows represent genes and columns represent samples. Rownames() must be accepted gene IDs.
metaginfo	Pathways object
sel_assay	Character or integer, indicating the assay to be processed in the SummarizedExperiment. Only applied if genes_vals is a SummarizedExperiment.Default is 1.
decompose	Boolean, whether to compute the values for the decomposed subpathways. By default, effector subpathways are computed.
maxnum	Number of maximum iterations when iterating the signal through the loops into the pathways
verbose	Boolean, whether to show details about the results of the execution of hipathia
tol	Tolerance for the difference between two iterations when iterating the signal through the loops into the pathways
test	Boolean, whether to test the input objects. Default is TRUE.

Value

A MultiAssayExperiment object with the level of activation of the subpathways from the pathways in pathigraphs for the experiment with expression values in genes_vals.

22 is_accepted_species

Examples

```
data(exp_data)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
results <- hipathia(exp_data, pathways, verbose = TRUE)
## Not run: results <- hipathia(exp_data, pathways, decompose = TRUE,
    verbose = FALSE)
## End(Not run)</pre>
```

igraphs_upgrade

Upgrade igraphs to current version

Description

Upgrades the igraph objects in metaginfo object to the corresponding version of the igraph package.

Usage

```
igraphs_upgrade(metaginfo)
```

Arguments

metaginfo

Pathways object

Value

The pathways object with the upgraded igraph objects

is_accepted_species

Checks whether a species is accepted

Description

Checks whether a species is accepted

Usage

```
is_accepted_species(species)
```

Arguments

species

Species of the samples.

#@examples #is_accepted_species("hsa") #is_accepted_species("fca")

Value

Boolean, whether species is accepted or not.

load_annofuns 23

load_annofuns

Loads annotations object

Description

Loads annotations object

Usage

```
load_annofuns(db, species)
```

Arguments

db Database to be used. Either "GO" or "uniprot".

species Species of the samples.

#@examples #load_annofuns("GO", "hsa") #load_annofuns("uniprot", "hsa")

Value

Annotations object

load_annots

Loads functional annotations to genes

Description

Loads functional annotations from HGNC to the selected database.

Usage

```
load_annots(db, species)
```

Arguments

db Database to be used. Either "GO" or "uniprot".

species Species of the samples.

#@examples #load_annots("GO", "hsa")

Value

Functional annotations from HGNC to the selected database.

24 load_gobp_frame

load_entrez_hgnc

Loads table of translation from HGNC to Entrez

Description

Loads table of translation from HGNC to Entrez

Usage

```
load_entrez_hgnc(species)
```

Arguments

species

Species of the samples.

#@examples #load_entrez_hgnc("hsa")

Value

Table of translation from HGNC to Entrez

load_gobp_frame

Loads GO graph information

Description

```
#@examples #load_gobp_frame()
```

Usage

```
load_gobp_frame()
```

Value

GO graph information

load_gobp_net 25

load_gobp_net

Loads GO graph

Description

```
#@examples #load_gobp_net()
```

Usage

```
load_gobp_net()
```

Value

GO graph

load_mgi

Loads object with graph information

Description

Loads object with graph information

Usage

```
load_mgi(species)
```

Arguments

species

Species of the samples.

#@examples #load_mgi("hsa")

Value

Graph information object

26 load_pathways

load_pathways

Loads the pathways object.

Description

Loads the pathways object, which includes information about the pathways to be analyzed.

Usage

```
load_pathways(species, pathways_list = NULL)
```

Arguments

species Species of the samples.

pathways_list Vector of the IDs of the pathways to load. By default all available pathways are

load.

Details

The object of pathways includes information about the pathways and the subpathways which will be analyzed. This object must be provided to some of the functions (like hipathia or quantify_terms) in the package. These functions will analyze all the pathways included in this object. By default, all available pathways are load. In order to restrict the analysis to a predefined set of pathways, specify the set of pathways to load with the parameter pathways_list.

Value

An pathways object including * species Species to which the pathways are related. * pathigraphs List of Pathigraph objects. Each Pathigraph contains the necessary information of a pathway for it to be analyzed with Hipathia. * all_genes List of all the genes included in the selection of pathways stored in pathigraphs. * eff_norm Vector of normalization values for effector subpathways. * path_norm Vector of normalization values for decomposed subpathways.

```
## Not run: pathways <- load_pathways("hsa")  # Loads all pathways for human
pathways <- load_pathways("mmu", c("mmu03320", "mmu04024", "mmu05200"))
  # Loads pathways 03320, 04024 and 05200 for mouse</pre>
```

load_pseudo_mgi 27

load_pseudo_mgi

Loads object with pseudo graph information

Description

Loads object with pseudo graph information

Usage

```
load_pseudo_mgi(species, group_by)
```

Arguments

species

Species of the samples.

group_by

How to group the subpathways to be visualized. By default they are grouped by the pathway to which they belong. Available groupings include "uniprot", to group subpathways by their annotated Uniprot functions, "GO", to group subpathways by their annotated GO terms, and "genes", to group subpathways by

the genes they include.

#@examples #load_pseudo_mgi("hsa", "uniprot")

Value

Pseudo graph information object

load_xref

Loads table of references

Description

Loads table of references

Usage

load_xref(species)

Arguments

species

Species of the samples.

#@examples #load_xref("hsa")

Value

Table of references

28 multiple_pca_plot

		r		_	٠	r
mg	i	f.	rom	S	i	f

Create a Pathways object from SIF files

Description

Creates a Pathways object from the information of a pathway stored in a SIF file with some attributes. This pathways object can be used by function hipathia to analyze data.

Usage

```
mgi_from_sif(sif.folder, spe, entrez_symbol = NULL, dbannot = NULL)
```

Arguments

sif.folder Path to the folder in which SIF and ATT files are stored.

spe Species

entrez_symbol Relation between Entrez (NCBI) genes and gene symbols. Data.frame with 2

columns: First column is the EntrezGene ID, second column is the gene Symbol. The genes in the nodes of the pathways should be defined by Entrez IDs in the SIF and ATT files of the pathways. In order to be more readable, gene names

are used when plotting the pathways.

dbannot Functional annotation of the genes in the pathways to create function nodes.

Value

A pathways object with the same structure of that returned by function load_pathways.

multiple_pca_plot

Plots multiple components of a PCA

Description

Plots multiple components of a PCA analysis computed with do_pca

Usage

```
multiple_pca_plot(
   fit,
   group = NULL,
   sample_colors = NULL,
   comps = seq_len(3),
   plot_variance = FALSE,
   legend = TRUE,
   cex = 2,
   pch = 20,
```

node_color 29

```
main = "Multiple PCA plot",
  save_png = NULL
)
```

Arguments

fit princomp object as returned by do_pca

group Vector with the group to which each sample belongs. The samples must be

ordered as in path_vals. By default, all samples will be assigned to the same

class.

sample_colors Named character vector of colors. The names of the colors must be the classes

in group. Each sample will be assigned the color corresponding to its class, taken from the group vector. By default a color will be assigned automatically

to each class.

comps Vector with the components to be plot

plot_variance Logical, whether to plot the cumulative variance.

legend Boolean, whether to plot a legend in the plot. Default is TRUE.

cex Graphical parameter from par() function.
pch Graphical parameter from par() function.

main Main title of the image

save_png Path to the file where the image as PNG will be saved. By default, the image is

not saved.

Value

Plots multiple components of a PCA

Examples

```
data(path_vals)
sample_group <- brca_design[colnames(path_vals),"group"]
pca_model <- do_pca(path_vals[seq_len(ncol(path_vals)),])
multiple_pca_plot(pca_model, sample_group, cex = 3, plot_variance = TRUE)</pre>
```

node_color

Get colors of the nodes from a comparison file

Description

Computes the colors of the nodes depending on the sign and p.value from the provided file. Significant up- and down-regulated nodes are depicted with the selected color, with a gradient towards the non-significant color depending on the value of the p-value. Smaller p-values give rise to purer colors than higher p-values.

30 node_color

Usage

```
node_color(
  comp,
  metaginfo,
  group_by = "pathway",
  colors = "classic",
  conf = 0.05,
  adjust = TRUE
)
```

Arguments

comp Comparison file as returned by do_wilcoxon. Must include a column named

"UP/DOWN" with the sign of the comparison coded as UP or DOWN, a column named "p.value" of raw p.values and a column named "FDRp.value" of adjusted

p.values.

metaginfo Object of pathways.

group_by How to group the subpathways to be visualized. By default they are grouped

by the pathway to which they belong. Available groupings include "uniprot", to group subpathways by their annotated Uniprot functions, "GO", to group subpathways by their annotated GO terms, and "genes", to group subpathways by

the genes they include. Default is set to "pathway".

colors Either a character vector with 3 colors (indicating, in this order, down-regulation,

non-significance and up-regulation colors) or a key name indicating the color

scheme to be used. Options are:

conf Level of significance of the comparison for the adjusted p-value.

adjust Boolean, whether to adjust the p.value from the comparison. Default is TRUE.

Value

List of color vectors, named by the pathways to which they belong. The color vectors represent the differential expression of the nodes in each pathway.

Slots

classic ColorBrewer blue, white and colorBrewer red.

hipathia Hipathia predefined color scheme: Green, white and orange. By default classic color scheme is applied.

```
data(results)
data(brca)
pathways_list <- c("hsa03320", "hsa04012")
pathways <- load_pathways(species = "hsa", pathways_list)
comp <- do_wilcoxon(results[["nodes"]], "group", "Tumor", "Normal")
colors_de <- node_color(comp, pathways)</pre>
```

node_color_per_de 31

node_color_per_de

Colors of the nodes by its differential expression

Description

Performs a Limma differential expression on the nodes and computes the colors of the nodes depending on it_ Significant up- and down-regulated nodes are depicted with the selected color, with a gradient towards the non-significant color depending on the value of the p-value. Smaller p-values give rise to purer colors than higher p-values.

Usage

```
node_color_per_de(
  results,
  metaginfo,
  group,
  expdes,
  g2 = NULL,
  group_by = "pathway",
  colors = "classic",
  conf = 0.05,
  adjust = TRUE
)
```

Arguments

resul	lts	Object of results as provided by the hipathia function_
metag	ginfo	Object of pathways_
group)	Character indicating the column in which the group variable is stored, in case the object provided to hipathia was a SummarizedExperiment, or a vector with the class to which each sample belongs. Samples must be ordered as in results.
expde	es	String, either the comparison to be performed or the label of the first group to be compared.
g2		String, label of the second group to be compared. Only necessary in case expdes is the name of the first group, not the comparison.
group	o_by	How to group the subpathways to be visualized. By default they are grouped by the pathway to which they belong. Available groupings include "uniprot", to group subpathways by their annotated Uniprot functions, "GO", to group subpathways by their annotated GO terms, and "genes", to group subpathways by the genes they include. Default is set to "pathway".
color	^s	Either a character vector with 3 colors (indicating, in this order, down-regulation, non-significance and up-regulation colors) or a key name indicating the color scheme to be used. Options are:
conf		Level of significance of the comparison for the adjusted p-value.
adjus	st	Boolean, whether to adjust the p.value from the comparison. Default is TRUE.

32 normalize_data

Value

List of color vectors, named by the pathways to which they belong. The color vectors represent the differential expression of the nodes in each pathway.

Slots

classic ColorBrewer blue, white and colorBrewer red.

hipathia Hipathia predefined color scheme: Green, white and orange. By default classic color scheme is applied.

Examples

```
data(results)
data(brca)
pathways_list <- c("hsa03320", "hsa04012")
pathways <- load_pathways(species = "hsa", pathways_list)
colors_de <- node_color_per_de(results, pathways, "group", "Tumor - Normal")
colors_de <- node_color_per_de(results, pathways, "group", "Tumor", "Normal")</pre>
```

normalize_data

Normalize expression data from a SummarizedExperiment or matrix to be used in hipathia

Description

Transforms the rank of the SummarizedExperiment or matrix of gene expression to [0,1] in order to be processed by hipathia. The transformation may be performed in two different ways. If percentil = FALSE, the transformation is a re-scaling of the rank of the matrix. If percentil = TRUE, the transformation is performed assigning to each cell its percentil in the corresponding distribution. This option is recommended for distributions with very long tails.

Usage

```
normalize_data(
  data,
  sel_assay = 1,
  by_quantiles = FALSE,
  by_gene = FALSE,
  percentil = FALSE,
  truncation_percentil = NULL
)
```

normalize_data 33

Arguments

data	Either a SummarizedExperiment or a matrix of gene expression.
sel_assay	Character or integer, indicating the assay to be normalized in the Summarized-Experiment. Default is 1.
by_quantiles	Boolean, whether to normalize the data by quantiles. Default is FALSE.
by_gene	Boolean, whether to transform the rank of each row of the matrix to $[0,1]$. Default is FALSE.
percentil	Boolean, whether to take as value the percentil of each sample in the corresponding distribution.
truncation_perd	centil
	Real number p in [0,1]. When provided, values beyond percentil p are truncated to the value of percentil p, and values beyond 1-p are truncated to percentil 1-p. By default no truncation is performed.

Details

This transformation may be applied either to the whole matrix (by setting by_gene = FALSE), which we strongly recommend, or to each of the rows (by setting by_gene = TRUE), allowing each gene to have its own scale.

A previous quantiles normalization may be applied by setting by_quantiles = TRUE. This is recommended for noisy data.

For distributions with extreme outlayer values, a percentil p may be given to the parameter truncation_percentil. When provided, values beyond percentil p are truncated to the value of percentil p, and values beyond 1-p are truncated to percentil 1-p. This step is performed before any other tranformation. By default no truncation is performed.

Value

Matrix of gene expression whose values are in [0,1].

```
data("brca_data")
trans_data <- translate_data(brca_data, "hsa")
exp_data <- normalize_data(trans_data)
exp_data <- normalize_data(trans_data, by_quantiles = TRUE,
truncation_percentil=0.95)</pre>
```

34 paths_to_go_ancestor

normalize_paths

Normalize the pathway matrix by rows

Description

Due to the nature of the Hipathia method, the length of a pathway may influence its signal rank. In order to compare signal values among subpathways, we strongly recommend to normalize the matrix with this normalization.

Usage

```
normalize_paths(path_vals, metaginfo)
```

Arguments

path_vals SummarizedExperiment or matrix of the pathway values

metaginfo Pathways object

Details

This function removes the bias caused by the length of the subpathways by dividing by the value obtained from running the method with a basal value of 0.5 at each node.

Value

SummarizedExperiment or matrix of normalized pathway values, depending on the class of path_vals.

Examples

```
data(path_vals)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
   "hsa04012"))
path_normalized <- normalize_paths(path_vals, pathways)</pre>
```

paths_to_go_ancestor

Create path results table with highest significant GO ancestors

Description

Create table of results with the comparison of the paths together with the GO functional annotation and the highest significant GO ancestor (HSGOA).

Usage

```
paths_to_go_ancestor(pathways, comp_paths, comp_go, pval = 0.05)
```

Arguments

pathways Pathways object

comp_paths Wilcoxon comparison of the matrix of pathways values as returned by do_wilcoxon.

comp_go Wilcoxon comparison of the matrix of GO values as returned by do_wilcoxon.

pval P-value cut-off. Default values is set to 0.05.

Details

The table returns in each row: the name of a pathway and its Wilcoxon comparison information (direction, adjusted p-value), the GO term to which the path is related (not necessarily unique), the Wilcoxon comparison information of this GO (direction, adjusted p-value), the HSGOA of this GO and its Wilcoxon comparison information (direction, adjusted p-value).

The HSGOA is computed as the GO term with minimum level from all the significant (with respect to value pval) ancestors of a GO. The level of a GO term is computed as the number of nodes in the shortest path from this GO term to the term "GO:0008150". The ancestors of a node are defined as all the nodes from which a path can be defined from the ancestor to the node.

Value

Table of comparisons with Highest common ancestors

Examples

```
data(comp)
data(go_vals)
data(brca_design)
data(path_vals)
sample_group <- brca_design[colnames(path_vals),"group"]
comp_go <- do_wilcoxon(go_vals, sample_group, g1 = "Tumor", g2 = "Normal")
## Not run: pathways <- load_pathways(species = "hsa", pathways_list =
c("hsa03320", "hsa04012"))
table <- paths_to_go_ancestor(pathways, comp, comp_go)
## End(Not run)</pre>
```

```
pathway_comparison_plot
```

Plots pathway with colored significant paths

Description

Plots the layout of a pathway, coloring the significant subpathways in different colors depending on whether they are significantly up- or down-regulated. Nodes may be also colored providing a suitable list of colors for each node. Function node_color_per_de assigns colors to the nodes depending on their differential expression.

Usage

```
pathway_comparison_plot(
  comp,
  metaginfo,
  pathway,
  conf = 0.05,
  node_colors = NULL,
  colors = "classic"
)
```

Arguments

comp Comparison data frame as returned by the do_wilcox function.

metaginfo Pathways object.

pathway Name of the pathway to be plotted.

conf Level of significance of the comparison for the adjusted p-value. Default is 0.05. node_colors List, named by the pathway name, including the color of each node for each

pathway.

colors Either a character vector with 3 colors (indicating, in this order, down-regulation,

non-significance and up-regulation colors) or a key name indicating the color

scheme to be used. Options are:

Value

Image in which a pathway is ploted. Edges are colored so that the UP- and DOWN-activated subpathways are identified.

Slots

classic ColorBrewer blue, white and colorBrewer red.

hipathia Hipathia predefined color scheme: Green, white and orange. By default classic color scheme is applied.

```
data(comp)
pathways_list <- c("hsa03320", "hsa04012")
pathways <- load_pathways(species = "hsa", pathways_list)
pathway_comparison_plot(comp, metaginfo = pathways, pathway = "hsa03320")

## Not run:
data(results)
data(brca)
colors_de <- node_color_per_de(results, pathways, group, "Tumor", "Normal")
pathway_comparison_plot(comp, metaginfo = pathways, pathway = "hsa04012",
node_colors = colors_de)

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

path_vals 37

path_vals

Pathways matrix of the BRCA gene expression dataset

Description

Matrix of pathway activation values for the BRCA dataset. This matrix is extracted from the Results object returned by the hipathia function by means of the get_paths_matrix function.

Usage

```
data(path_vals)
```

Format

Matrix with 40 columns and 1868 rows. Row names are Pathway IDs and column names are the TCGA identifyers of the samples.

Details

```
path_vals <- get_paths_matrix(results)</pre>
```

Value

Matrix with 40 columns and 1868 rows. Row names are Pathway IDs and column names are the TCGA identifyers of the samples.

pca_plot

Plots two components of a PCA

Description

Plots two components of a PCA computed with do_pca

Usage

```
pca_plot(
   fit,
   group = NULL,
   sample_colors = NULL,
   cp1 = 1,
   cp2 = 2,
   legend = TRUE,
   legend_xy = "bottomleft",
   cex = 2,
   pch = 20,
   mgp = c(3, 1, 0),
```

pca_plot

```
main = "PCA plot",
  save_png = NULL
)
```

Arguments

fit	princomp object as returned by do_pca
group	Vector with the group to which each sample belongs. The samples must be ordered as in rownames(fit\$scores). By default, all samples will be assigned to the same class.
sample_colors	Named character vector of colors. The names of the colors must be the classes in group. Each sample will be assigned the color corresponding to its class, taken from the group vector. By default a color will be assigned automatically to each class.
cp1	Integer, number of the component in the X-axis. Default is 1, the first component.
cp2	Integer, number of the component in the Y-axis. Default is 2, the second component.
legend	Boolean, whether to plot a legend in the plot. Default is TRUE.
legend_xy	Situation of the legend in the plot. Available options are: "bottomright", "bottom", "bottomleft", "left", "topleft", "topright", "right" and "center".
cex	Graphical parameter from par() function.
pch	Graphical parameter from par() function.
mgp	Graphical parameter from par() function.
main	Title of the graphics
save_png	Path to the file where the image as PNG will be saved. By default, the image is

Value

Plots two components of a PCA

not saved.

```
data(path_vals)
sample_group <- brca_design[colnames(path_vals),"group"]
pca_model <- do_pca(path_vals[seq_len(ncol(path_vals)),])
pca_plot(pca_model, sample_group)</pre>
```

quantify_terms 39

quantify_terms	Computes the level of activation of the functions related to the previously computed subpathways

Description

Computes the level of activation of the functions related to the previously computed subpathways

Usage

```
quantify_terms(
  results,
  metaginfo,
  dbannot,
  out_matrix = FALSE,
  normalize = TRUE
)
```

Arguments

metaginfo Pathways object

dbannot Either a string indicating which precomputed annotation to use ("uniprot" for

Uniprot Keywords or "GO" for Gene Ontology terms), or a dataframe with the annotation of the genes to the functions. First column are gene symbols, second

column the functions.

out_matrix Boolean, whither the output object should be a matrix object. Default is FALSE,

returning a SummarizedExperiment object.

normalize Boolean, whether to normalize the matrix of pathway values with normalize_paths

before quantifying the signal. Due to the nature of the Hipathia method, in which the length of each pathway may alter its signal rank, we strongly recommend to perform this normalization. This normalization removes the bias. Default is set

to TRUE.

Value

Matrix with the level of activation of the functions in dbannot

```
data(results)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
   "hsa04012"))
go_values <- quantify_terms(results, pathways, "GO")
uniprot_values <- quantify_terms(results, pathways, "uniprot")</pre>
```

40 save_results

results	Results object	

Description

Results object returned by hipathia::hipathia function, after calling results <- hipathia(exp_data, pathways, verbose=TRUE)

Usage

```
data(results)
```

Format

Object of results, including pathways information.

Value

Object of results, including pathways information.

save_results	Save results to folder	

Description

Saves results to a folder. In particular, it saves the matrix of subpathway values, a table with the results of the provided comparison, the accuracy of the results and the .SIF and attributes of the pathways.

Usage

```
save_results(results, comp, metaginfo, output_folder = NULL, path = NULL)
```

Arguments

results Results object as returned by the hipathia function.

comp Comparison as returned by the do_wilcoxon function.

metaginfo Pathways object

output_folder Name of the folder in which the results will be stored.

path Absolute path to the parent directory in which 'output_folder' will be saved. If

it is not provided, it will be created in a temp folder.

Value

Creates a folder in disk in which all the information to browse the pathway results is stored.

top_pathways 41

Examples

```
data(results)
data(comp)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
save_results(results, comp, pathways, "output_results")</pre>
```

top_pathways

Computes pathway significance

Description

Performs a test for each pathway checking if the number of significant paths is significant, compared to not having any of the paths as significant.

Usage

```
top_pathways(comp)
```

Arguments

comp

Comparison data frame as returned by the do_wilcoxon function.

Value

Table with the names of the pathways and their p-value for the Fisher test comparing the proportion of significant subpaths vs. 0.

Examples

```
data(comp)
top_pathways(comp)
```

translate_data

Translation of the rownames IDs of a SummarizedExperiment to Entrez IDs.

Description

Translates the IDs in the rownames of a SummarizedExperiment to Entrez IDs. For accepted IDs to be transformed see the DOCUMENTATION.

Usage

```
translate_data(data, species, sel_assay = 1, verbose = TRUE)
```

42 translate_matrix

Arguments

data Either a SummarizedExperiment object or a matrix of gene expression.

species Species of the samples.

sel_assay Character or integer, indicating the assay to be translated in the SummarizedEx-

periment. Default is 1.

verbose Boolean, whether to show details about the results of the execution.

Value

Either a SummarizedExperiment or a matrix (depending on the input type) of gene expression with Entrez IDs as rownames.

Examples

```
data("brca_data")
trans_data <- translate_data(brca_data, "hsa")</pre>
```

translate_matrix

Translation of the rownames IDs of a matrix to Entrez IDs.

Description

Translates the IDs in the rownames of a matrix to Entrez IDs. For accepted IDs to be transformed see the DOCUMENTATION.

Usage

```
translate_matrix(exp, species, verbose = TRUE)
```

Arguments

exp Matrix of gene expression.

species Species of the samples.

verbose Boolean, whether to show details about the results of the execution.

Value

Matrix of gene expression with Entrez IDs as rownames.

visualize_report 43

visualize_report

Visualize a HiPathia report

Description

Visualize a HiPathia report

Usage

```
visualize_report(output_folder, port = 4000)
```

Arguments

```
output_folder Folder in which results to visualize are stored port Port to use
```

Value

The instructions to visualize a HiPathia report in a web browser

```
data(comp)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320",
    "hsa04012"))
report <- create_report(comp, pathways, "save_results")
visualize_report(report)

## Not run:
data(results)
data(brca)
sample_group <- colData(brca)[,1]
colors_de <- node_color_per_de(results, pathways,
    sample_group, "Tumor", "Normal")
report <- create_report(comp, pathways, "save_results",
    node_colors = colors_de)
visualize_report(report)
visualize_report(report, port = 5000)

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

Index

* datasets	is_accepted_species, 22
brca, 4	
brca_data, 4	load_annofuns, 23
brca_design,5	load_annots, 23
comp, 6	<pre>load_entrez_hgnc, 24</pre>
exp_data, 9	<pre>load_gobp_frame, 24</pre>
go_vals, 18	load_gobp_net, 25
path_vals, 37	load_mgi, 25
results, 40	load_pathways, 26
	load_pseudo_mgi, 27
annotate_paths, 3	load_xref,27
brca, 4	mgi_from_sif, 28
brca_data, 4	multiple_pca_plot, 28
brca_design,5	
	node_color, 29
comp, 6	node_color_per_de, 31
create_report, 6	normalize_data, 32
da nas 7	normalize_paths, 34
do_pca, 7	path_vals, 37
do_wilcoxon, 8	path_vals, 37 paths_to_go_ancestor, 34
exp_data, 9	pathway_comparison_plot, 35
cxp_uatu, >	pca_plot, 37
get_go_names, 10	ped_p100, 07
<pre>get_highest_sig_ancestor, 11</pre>	quantify_terms, 39
<pre>get_node_names, 12</pre>	
get_nodes_data, 11	results, 40
<pre>get_path_names, 17</pre>	7. 40
get_paths_data, 13	save_results,40
<pre>get_pathway_functions, 16</pre>	top_pathways, 41
<pre>get_pathways_annotations, 14</pre>	translate_data,41
<pre>get_pathways_list, 15</pre>	translate_matrix, 42
<pre>get_pathways_summary, 15</pre>	ti alistate_mati 1x, 42
go_vals, 18	visualize_report,43
heatmap_plot, 18	
hhead, 20	
hipathia, 21	
igraphs_upgrade, 22	