# Package ‘hipathia’

**February 20, 2024**

**Title**  HiPathia: High-throughput Pathway Analysis  

**Version**  3.2.0  

**Description**  Hipathia is a method for the computation of signal transduction along 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 (>= 4.1), igraph (>= 1.0.1), AnnotationHub(>= 2.6.5), MultiAssayExperiment(>= 1.4.9), SummarizedExperiment(>= 1.8.1)  

**License**  GPL-2  

**Encoding**  UTF-8  

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**annotate_paths**

Annotates functions to pathways

---

**Description**

Annotates functions from a database to each pathway

**Usage**

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

**Arguments**

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>metaginfo</td>
<td>Pathways object</td>
</tr>
<tr>
<td>dbannot</td>
<td>Either a string indicating which precomputed annotation to use (&quot;uniprot&quot; for Uniprot Keywords or &quot;GO&quot; 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.</td>
</tr>
</tbody>
</table>
Value

Object of annotations from pathways to functions

```
# @examples
# pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320", ":hsa04012"))
# annotate_paths(pathways, "GO")
# @export
```

---

`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 identifiers 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 identifiers of the samples.

Source

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

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

**Usage**
data(brca_data)

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

**Source**
https://cancergenome.nih.gov/

---

**brca_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/

<table>
<thead>
<tr>
<th>comp</th>
<th>Wilcoxon comparison of pathways object</th>
</tr>
</thead>
</table>

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

<table>
<thead>
<tr>
<th>create_report</th>
<th>Create visualization HTML</th>
</tr>
</thead>
</table>

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.
create_report

Usage

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

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")
DAcomp <- create_report(comp, pathways, "save_results",
node_colors = colors_de)

# End(Not run)

DAcomp

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compares the gene expression, pathway activation level and the function activation level of the</td>
</tr>
</tbody>
</table>

### Usage

```r
DAcomp(
  hidata,
  groups,
  expdes,
  g2 = NULL,
  path.method = "wilcoxon",
  node.method = "limma",
  fun.method = "wilcoxon",
  order = FALSE,
  paired = FALSE,
  adjust = TRUE,
  conf.level = 0.05,
  sel_assay = 1
)
```

### Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>hidata</td>
<td>Either a SummarizedExperiment object or a matrix, returned by function hipathia.</td>
</tr>
<tr>
<td>groups</td>
<td>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 hidata.</td>
</tr>
<tr>
<td>expdes</td>
<td>String, either an equation expression to pass to limma, or the label of the first group to be compared</td>
</tr>
<tr>
<td>g2</td>
<td>String, label of the second group to be compared, if not specified in expdes.</td>
</tr>
<tr>
<td>path.method</td>
<td>String, method to be used when comparing pathways. Options include wilcoxon (default, performs a Wilcoxon test comparing conditions expdes and g2 - in this case, mandatory parameter) and limma (performs a limma DE analysis using functions lmFit, contrasts.fit and eBayes using the formula in expdes or comparing conditions expdes and g2.</td>
</tr>
</tbody>
</table>
node.method  String, method to be used when comparing nodes. Options include `wilcoxon` (performs a Wilcoxon test comparing conditions `expdes` and `g2` - in this case, mandatory parameter) and `limma` (default, performs a limma DE analysis using functions `lmFit`, `contrasts.fit` and `eBayes` using the formula in `expdes` or comparing conditions `expdes` and `g2`).

fun.method  String, method to be used when comparing functions. Options include `wilcoxon` (default, performs a Wilcoxon test comparing conditions `expdes` and `g2` - in this case, mandatory parameter) and `limma` (performs a limma DE analysis using functions `lmFit`, `contrasts.fit` and `eBayes` using the formula in `expdes` or comparing conditions `expdes` and `g2`).

order  Boolean, whether to order the results table by the `FDRp.value` column. Default is FALSE.

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. Default is TRUE.

cnf.level  Numeric, cut off for significance. Default is 0.05.

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

Value

List including comparison results for nodes, pathways and functions, if present.

Examples

data(hidata)
comp <- DAcomp(hidata, groups = "group", expdes = "Tumor", g2 = "Normal")

Description

Comparison object returned by `hipathia::DAcomp` function, after calling `DAdata <- DAcomp(hidata, "group", g1 = "Tumor", g2 = "Normal")`

Usage

data(DAdata)
Format

List object with 4 entries: Nodes includes a matrix with 6826 rows and 8 columns Paths includes a matrix with 1876 rows and 13 columns Uni.terms includes a matrix with 142 rows and 6 columns GO.terms includes a matrix with 1654 rows and 6 columns

Value

List of tibbles with the comparison results

---

**DAoverview**

*Table and plot of total number of altered and not altered nodes, paths and functions (Uniprot keywords and/or GO terms, if present).*

Description

Table and plot of total number of altered and not altered nodes, paths and functions (Uniprot keywords and/or GO terms, if present).

Usage

```
DAoverview(DAdata, conf.level = 0.05, adjust = TRUE, colors = "hiro")
```

Arguments

- **DAdata**: List of comparison results, returned by function `DAcomp`.
- **conf.level**: Numeric, cut off for significance. Default is 0.05.
- **adjust**: Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method. Default is TRUE.
- **colors**: String with the color scheme or vector of colors to be used. See `define_colors` for available options. Default is "hiro".

Value

Plot and tibble including the number of total, altered, UP- and DOWN-regulated features for nodes, paths and functions if present.

Examples

```
data(DAdata)
DAoverview(DAdata)
```
**DAreport**

*Create visualization HTML*

**Description**

Saves the results of a DAdata 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**

```r
DAreport(
    DAdata,
    pathways,
    conf.level = 0.05,
    adjust = TRUE,
    group_by = "pathway",
    colors = "classic",
    output_folder = NULL,
    path = NULL,
    verbose = TRUE
)
```

**Arguments**

- **DAdata**: List of comparison results, returned by function DAcomp.
- **pathways**: Pathways object as returned by the load_pathways function
- **conf.level**: Level of significance. By default 0.05.
- **adjust**: Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method. Default is TRUE.
- **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**: String with the color scheme or vector of colors to be used. See define_colors for available options. Default is "hiro".
- **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.
- **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

```r
data(DAdata)
data(pathways)
DAreport(DAdata, pathways)
```

---

**DAsummary**  
Lists and plots the top \( n \) altered pathways, taking into account the number of altered.

**Description**

Lists and plots the top \( n \) altered pathways, taking into account the number of altered.

**Usage**

```r
DAsummary(
  DAdata,
  n = 10,
  conf.level = 0.05,
  adjust = TRUE,
  ratio = FALSE,
  colors = "hiro",
  order.by = "number"
)
```

**Arguments**

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAdata</td>
<td>List of comparison results, returned by function DAcomp.</td>
</tr>
<tr>
<td>n</td>
<td>Number of top features to show.</td>
</tr>
<tr>
<td>conf.level</td>
<td>Numeric, cut off for significance. Default is 0.05.</td>
</tr>
<tr>
<td>adjust</td>
<td>Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method. Default is TRUE.</td>
</tr>
<tr>
<td>ratio</td>
<td>Boolean, whether to plot the ratio of significant paths with respect to the total paths in the pathway. Default is FALSE.</td>
</tr>
<tr>
<td>colors</td>
<td>String with the color scheme or vector of colors to be used. See define_colors for available options. Default is &quot;hiro&quot;.</td>
</tr>
<tr>
<td>order.by</td>
<td>String, how to order table of results. Available options include ratio (default, uses the ratio of significant paths with respect to the total paths in the pathway) and number (uses the number of significant paths in the pathway).</td>
</tr>
</tbody>
</table>

**Value**

Plot and tibble including top \( n \) altered pathways.
**Examples**

```r
data(DAdata)
DAsummary(DAdata)
```

---

**DAtop**

Lists and plots the top n altered nodes, paths and functions (Uniprot keywords and/or GO terms, if present).

**Description**

Lists and plots the top n altered nodes, paths and functions (Uniprot keywords and/or GO terms, if present).

**Usage**

```
DAtop(DAdata, n = 10, conf.level = 0.05, adjust = TRUE, colors = "hiro")
```

**Arguments**

- **DAdata**: List of comparison results, returned by function DAcomp.
- **n**: Number of top features to show.
- **conf.level**: Numeric, cut off for significance. Default is 0.05.
- **adjust**: Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method. Default is TRUE.
- **colors**: String with the color scheme or vector of colors to be used. See define_colors for available options. Default is "hiro".

**Value**

Plot and list of tables including top n altered features for nodes, paths and functions if present.

**Examples**

```r
data(DAdata)
DAtop(DAdata)
```
define_colors  
*Color palettes to be used in plots.*

**Description**

Color palettes to be used in plots.

**Usage**

```r
define_colors(colors, no.col = NULL)
```

**Arguments**

- **colors**  
  String with the color scheme or vector of colors to be used. Available predefined options include: hipathia, classic, soft, okee, hiro, new, vg, orchid.

- **no.col**  
  String with the color given to non-significant nodes, if not given in parameter colors.

**Value**

Plot and list of tables including top n altered features for nodes, paths and functions if present.

**Examples**

```r
define_colors("hiro")
```

do_pca  
*Performs a Principal Components Analysis*

**Description**

Performs a Principal Components Analysis

**Usage**

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

**Arguments**

- **data**  
  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 SummarizedExperiment. 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.)
do_wilcoxon

Value

do_pca returns a list with class princomp.

Examples

data(path_vals)
pca_model <- do_pca(path_vals[seq_len(ncol(path_vals)),])

---

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
)

Arguments

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 wilcoxon_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")

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.

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

Translates GO IDs to GO names

Description

Translates the GO IDs to readable and comprehensible names.

Usage

get_go_names(names, species, maxchar = NULL, disambiguate = FALSE)

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.

Examples

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
)


**get Nodes Data**

**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 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 `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.

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**

```r
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.
get_node_names

Examples

```r
data(results)
path_vals <- get_paths_data(results)
```

get_node_names  

**Tranlates node IDs to node names**

Description

Translates the node IDs to readable and comprehensible 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

```r
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.

Value

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

Examples

```r
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))
```
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)
**get_pathways_annotations**

*Get Pathways functional annotations*

**Description**

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

**Usage**

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

**Arguments**

- `pathway_names`: Character vector of the names of the pathways
- `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`.

**Examples**

```r
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320", "hsa04012"))
## Not run: get_pathways_annotations(pathway_names, pathways, "GO")
gapathways_annotations(pathway_names, pathways, "uniprot")
```
### get_pathways_list

**Description**

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

**Usage**

```r
get_pathways_list(metaginfo)
```

**Arguments**

- `metaginfo`: Pathways object

**Value**

List of the pathway IDs included in the pathways object

**Examples**

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

### get_pathways_summary

**Description**

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

**Usage**

```r
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.
get_pathway_functions

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)

---

get_pathway_functions  Returns functions related to a pathway

Description

Returns functions related to a pathway

Usage

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

Arguments

pathigraph  Pathway 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.
use_last_nodes  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

Value

List of annotations from pathways to functions

---

get_path_names  Translates path IDs to path names

Description

Translates the subpathway IDs to readable and comprehensible 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.

Examples

data(path_vals)
pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320", "hsa04012"))
translated_names <- get_path_names(pathways, rownames(path_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 identifiers of the samples.

**Details**
go_vals <- quantify_terms(results, pathways, "GO")

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

**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,
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 SummarizedExperiment. 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 rownames(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
Examples

```r
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)
```

---

**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**

```r
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.

**Examples**

```r
mat <- matrix(rnorm(100), ncol = 10)
hhead(mat)
hhead(mat, 3)
hhead(mat, 7)
```
hidata

Results object returned by hipathia::hipathia function, after calling hidata <- hipathia(brca, pathways, verbose=TRUE, uni.terms = TRUE, GO.terms = TRUE)

Usage

data(hidata)

Format

MultiAssayExperiment object of 4 listed experiments, with the activity values of nodes, paths and functional annotations for each sample: Nodes includes a matrix with 6826 rows Paths includes a matrix with 1876 rows Uni.terms includes a matrix with 142 rows GO.terms includes a matrix with 1654 rows

Value

Object of results, including nodes, pathways and functional information.

hipathia

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

Description

#@importFrom igraph

Usage

hipathia(
  genes_vals,
  metaginfo,
  uni.terms = FALSE,
  GO.terms = FALSE,
  sel_assay = 1,
  decompose = FALSE,
  scale = TRUE,
  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

uni.terms  Boolean, whether to compute functional analysis with Uniprot keywords.

GO.terms  Boolean, whether to compute functional analysis with Gene Ontology terms.

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.

scale  Boolean, whether to scale the values matrix to [0,1]. Default is TRUE.

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.

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)

igraphs_upgrade  Upgrade igraphs to current version

Description

Upgrades the igraph objects in metaginfo object to the corresponding version of the igraph pack-

age.
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.

Value

Boolean, whether species is accepted or not.

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.

Value

The pathways object with the upgraded igraph objects
load_annots

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.

load_entrez_hgnc

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_mgi

load_gobp_frame  Loads GO graph information

Description

  #@examples #load_gobp_frame()

Usage

  load_gobp_frame()

Value

  GO graph information

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")
load_pathways

Value

Graph information 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.

Examples

## Not run: pathways <- load_pathways("hsa") # Loads all pathways for human
paths <- load_pathways("mmu", c("mmu03320", "mmu04024", "mmu05200"))
# Loads pathways 03320, 04024 and 05200 for mouse
**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
**mgi_from_sif**  
*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**

```r
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**

```r
multiple_pca_plot(
  fit,
  group = NULL,
  sample_colors = NULL,
  comps = seq_len(3),
  plot_variance = FALSE,
  legend = TRUE,
  cex = 2,
  pch = 20,
)```
main = "Multiple PCA plot",
save_png = NULL
)

Arguments

fit          princomp object as returned by do_pca

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.

coms         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)

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.
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.

Examples

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

Arguments
- **results**: Object of results as provided by the `hipathia` function.
- **metaginfo**: 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`.
- **expdes**: 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_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.
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)
color_de <- node_color_per_de(results, pathways, "group", "Tumor - Normal")
color_de <- node_color_per_de(results, pathways, "group", "Tumor", "Normal")

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
)
Arguments

- **data**: Either a SummarizedExperiment or a matrix of gene expression.
- **sel_assay**: Character or integer, indicating the assay to be normalized in the SummarizedExperiment. 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_percentil**: 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 transformation. By default no truncation is performed.

Value

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

Examples

```r
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)
```
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)

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 for 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

```r
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)
```

| pathways | Pathways object including pathways has03320 and hsa04012. |

Description

Pathways object returned by `hipathia::load_pathways` function, after calling `pathways <- load_pathways(species = "hsa", pathways_list = c("hsa03320", "hsa04012"))`

Usage

```r
data(pathways)
```
**pathway_comparison_plot**

**Format**

Pathways object

**Value**

Pathways object including pathways has03320 and hsa04012.

**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**

```r
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 plotted. 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.

Examples

```r
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)

## End(Not run)
```

---

**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

```r
data(path_vals)
```

Format

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

Details

```r
path_vals <- get_paths_matrix(results)
```

Value

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

Plots two components of a PCA computed with do_pca

**Description**

Plots two components of a PCA computed with do_pca

**Usage**

```r
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),
  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", "top", "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 not saved.

Value
Plots two 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)),])
pca_plot(pca_model, sample_group)

plotVG

Plots a pathway with or without the comparison information, using the visNetwork library.

Description
Plots a pathway with or without the comparison information, using the visNetwork library.

Usage

plotVG(
  name,
  pathways,
  DAdata = NULL,
  colors = "hiro",
  conf = 0.05,
  adjust = TRUE,
  main = "Pathway",
  submain = "",
  no.col = "BlanchedAlmond",
  height = "800px"
)

Arguments

name KEGG ID of the pathway to plot.
pathways Pathways object.
DAdata List of comparison results, returned by function DAcomp.
colors String with the color scheme or vector of colors to be used. See define_colors for available options. Default is "hiro".
quantify_terms

    conf Numeric, cut off for significance. Default is 0.05.
    adjust Boolean, whether to adjust the p.value with Benjamini-Hochberg FDR method. Default is TRUE.
    main Title of the plot.
    submain Subtitle of the plot.
    no.col String with the color given to non-significant nodes.
    height Height of the plot. Default is "800px".

Value

Plot of the pathway.

Examples

data(pathways)
plotVG("hsa03320", pathways)

data(DAdata)
plotVG("hsa04012", pathways, DAdata)

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

results List of results as returned by the hipathia function
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, whether 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

Examples

```r
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")
```

---

**results**  
*Results object*

**Description**

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

**Usage**

```r
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.

Examples

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

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)

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 SummarizedExperiment. 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")
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**

```r
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  

Visualize a HiPathia report

**Description**

Visualize a HiPathia report

**Usage**

```r
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
Examples

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)
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