

# Package ‘hipathia’

April 16, 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 | <i>Annotates functions to pathways</i> |
|----------------|--|

---

**Description**

Annotates functions from a database to each pathway

**Usage**

```
annotate_paths(metainfo, dbannot)
```

**Arguments**

|          |  |
|----------|--|
| metainfo | 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

```
#@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 | <i>BRCA gene expression dataset</i> |
|-----------|-------------------------------------|

---

**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 | <i>BRCA experimental design</i> |
|-------------|---------------------------------|

---

**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/>

---

|      |   |
|------|---|
| comp | <i>Wilcoxon comparison of pathways object</i> |
|------|---|

---

**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 | <i>Create visualization HTML</i> |
|---------------|----------------------------------|

---

**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,
  metainfo,
  output_folder = NULL,
  path = NULL,
  node_colors = NULL,
  group_by = "pathway",
  conf = 0.05,
  verbose = FALSE
)
```

**Arguments**

|               |   |
|---------------|---|
| comp          | Comparison object as given by the <code>do_wilcoxon</code> function   |
| metainfo      | Pathways object as returned by the <code>load_pathways</code> 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 <code>node_color_per_de</code> 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)
```

---

|        |  |
|--------|--|
| DAcomp | <i>Compares the gene expression, pathway activation level and the function activation level of the</i> |
|--------|--|

---

## Description

Compares the gene expression, pathway activation level and the function activation level of the

## Usage

```
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

|             |   |
|-------------|---|
| hidata      | Either a SummarizedExperiment object or a matrix, returned by function <code>hipathia</code> .  |
| groups      | Either a character indicating the name of the column in <code>colData</code> including the classes to compare, or a character vector with the class to which each sample belongs. Samples must be ordered as in <code>hidata</code> .   |
| expdes      | String, either an equation expression to pas to <code>limma</code> , or the label of the first group to be compared   |
| g2          | String, label of the second group to be compared, if not specified in <code>expdes</code> .   |
| path.method | String, method to be used when comparing pathways. Options include <code>wilcoxon</code> (default, performs a Wilcoxon test comparing conditions <code>expdes</code> and <code>g2</code> - in this case, mandatory parameter) and <code>limma</code> (performs a <code>limma</code> DE analysis using functions <code>lmFit</code> , <code>contrasts.fit</code> and <code>eBayes</code> using the formula in <code>expdes</code> or comparing conditions <code>expdes</code> and <code>g2</code> ). |



|                          |   |
|--------------------------|---|
| <code>node.method</code> | String, method to be used when comparing nodes. Options include <code>wilcoxon</code> (performs a Wilcoxon test comparing conditions <code>expdes</code> and <code>g2</code> - in this case, mandatory parameter) and <code>limma</code> (default, performs a limma DE analysis using functions <code>lmFit</code> , <code>contrasts.fit</code> and <code>eBayes</code> using the formula in <code>expdes</code> or comparing conditions <code>expdes</code> and <code>g2</code> ).     |
| <code>fun.method</code>  | String, method to be used when comparing functions. Options include <code>wilcoxon</code> (default, performs a Wilcoxon test comparing conditions <code>expdes</code> and <code>g2</code> - in this case, mandatory parameter) and <code>limma</code> (performs a limma DE analysis using functions <code>lmFit</code> , <code>contrasts.fit</code> and <code>eBayes</code> using the formula in <code>expdes</code> or comparing conditions <code>expdes</code> and <code>g2</code> ). |
| <code>order</code>       | Boolean, whether to order the results table by the <code>FDRp.value</code> column. Default is <code>FALSE</code> .  |
| <code>paired</code>      | Boolean, whether the samples to be compared are paired. If <code>TRUE</code> , function <code>wilcoxsign_test</code> from package <code>coin</code> is used. If <code>FALSE</code> , function <code>wilcox.test</code> from package <code>stats</code> is used.   |
| <code>adjust</code>      | Boolean, whether to adjust the <code>p.value</code> with Benjamini-Hochberg FDR method. Default is <code>TRUE</code> .  |
| <code>conf.level</code>  | Numeric, cut off for significance. Default is 0.05.   |
| <code>sel_assay</code>   | 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")
```

---

|        |  |
|--------|--|
| DAdata | <i>Wilcoxon and limma comparison object for nodes, pathways and functional annotations</i> |
|--------|--|

---

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

---

**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**

```
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**

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

---

|           |  |
|-----------|--|
| DAsummary | <i>Lists and plots the top n altered pathways, taking into account the number of altered .</i> |
|-----------|--|

---

**Description**

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

**Usage**

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

**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.  |
| ratio      | Boolean, whether to plot the ratio of significant paths with respect to the total paths in the pathway. Default is FALSE.  |
| colors     | String with the color scheme or vector of colors to be used. See <code>define_colors</code> for available options. Default is "hiro".  |
| order.by   | String, how to order table of results. Available options include <code>ratio</code> (default, uses the ratio of significant paths with respect to the total paths in the pathway) and <code>number</code> (uses the number of significant paths in the pathway). |

**Value**

Plot and tibble including top n altered pathways.

**Examples**

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

---

|       |   |
|-------|---|
| DAtop | <i>Lists and plots the top n altered nodes, paths and functions (Uniprot keywords and/or GO terms, if present).</i> |
|-------|---|

---

**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**

```
data(DAdata)
DAtop(DAdata)
```

---

|               |  |
|---------------|--|
| define_colors | <i>Color palettes to be used in plots.</i> |
|---------------|--|

---

**Description**

Color palettes to be used in plots.

**Usage**

```
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**

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

---

|        |   |
|--------|---|
| do_pca | <i>Performs a Principal Components Analysis</i> |
|--------|---|

---

**Description**

Performs a Principal Components Analysis

**Usage**

```
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 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)),])
```

---

|             |                            |
|-------------|----------------------------|
| do_wilcoxon | <i>Apply Wilcoxon test</i> |
|-------------|----------------------------|

---

**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 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")
```

---

exp\_data

*Normalized BRCA gene expression dataset*

---

**Description**

Experimental design matrix once expression matrix brca\_data has been translated to Entrez genes 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 identifiers 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 identifiers of the samples.



---

|              |                                     |
|--------------|-------------------------------------|
| get_go_names | <i>Tranlates GO IDs to GO names</i> |
|--------------|-------------------------------------|

---

**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. |
| disambiguate | Boolean, whether to return unique strings by disambiguating with numbers.                         |

**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 | <i>Get highest common GO ancestor of GO annotations</i> |
|--------------------------|---|

---

**Description**

Get highest common GO ancestor of GO annotations

**Usage**

```
get_highest_sig_ancestor(
  go_terms,
  go_comp,
  metainfo,
  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.                            |
| metainfo | 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**

```
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)
```

---

|                |   |
|----------------|---|
| get_node_names | <i>Tranlates node IDs to node names</i> |
|----------------|---|

---

**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**

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

**Arguments**

|          |   |
|----------|---|
| metainfo | 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(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))
```

---

|                |  |
|----------------|--|
| get_paths_data | <i>Gets the object of subpathway activation values</i> |
|----------------|--|

---

### 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

|                      |  |
|----------------------|--|
| <code>results</code> | Results object as returned by <code>hipathia</code> .  |
| <code>matrix</code>  | Boolean, if TRUE the function returns a matrix object, if FALSE (as default) returns a <code>SummarizedExperiment</code> 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_annotatations`*Get Pathways functional annotations*

---

## Description

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

## Usage

```
get_pathways_annotatations(pathway_names, metainfo, dbannot, collapse = FALSE)
```

## Arguments

|                            |  |
|----------------------------|--|
| <code>pathway_names</code> | Character vector of the names of the pathways  |
| <code>metainfo</code>      | Pathways object  |
| <code>dbannot</code>       | 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. |
| <code>collapse</code>      | 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

```
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_annotatations(pathway_names, pathways, "GO")  
get_pathways_annotatations(pathway_names, pathways, "uniprot")
```

---

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 metainfo

**Usage**

```
get_pathways_list(metainfo)
```

**Arguments**

metainfo      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)
```

---

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, metainfo, conf = 0.05)
```

**Arguments**

comp      Comparison data frame as returned by the do\_wilcoxon function.  
metainfo      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 analyzed 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.   |

**Value**

List of annotations from pathways to functions

---

|                |   |
|----------------|---|
| get_path_names | <i>Tranlates path IDs to path names</i> |
|----------------|---|

---

**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(metainfo, names, maxchar = NULL)
```

**Arguments**

|          |   |
|----------|---|
| metainfo | 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))
```



---

`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 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.

---

`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,
```

```

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

```

### Arguments

|                             |  |
|-----------------------------|--|
| <code>data</code>           | Either a SummarizedExperiment or a matrix with the values to be plotted. Rows are features and columns are samples.  |
| <code>group</code>          | Either a character indicating the name of the column in <code>colData</code> including the classes to plot, or a character vector with the class to which each sample belongs. Samples must be ordered as in <code>data</code> . By default, all samples will be assigned to the same class.   |
| <code>sel_assay</code>      | Character or integer, indicating the assay to be normalized in the Summarized-Experiment. Default is 1.  |
| <code>colors</code>         | 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: * <code>classic</code> Blue for lower values, white for medium values, red for higher values. * <code>hipathia</code> Hipathia predefined color scheme: Green for lower values, white for medium values, orange for higher values. * <code>redgreen</code> Green for lower values, black for medium values, red for higher values. By default <code>classic</code> color scheme is applied. |
| <code>sample_clust</code>   | Boolean, whether to cluster samples (columns). By default TRUE.  |
| <code>variable_clust</code> | Boolean, whether to cluster variables (rows). By default FALSE. If TRUE, rows with 0 variance are removed.   |
| <code>labRow, labCol</code> | Character vectors with row and column labels to be used. By default <code>rownames(data)</code> or <code>colnames(data)</code> are used, respectively.   |
| <code>sample_colors</code>  | Named character vector of colors. The names of the colors must be the classes in <code>group</code> . Each sample will be assigned the color corresponding to its class, taken from the <code>group</code> vector. By default a color will be assigned automatically to each class.  |
| <code>scale</code>          | Boolean, whether to scale each row to the interval [0,1]. Default is TRUE.   |
| <code>save_png</code>       | Path to the file where the image as PNG will be saved. By default, the image is not saved.   |
| <code>legend</code>         | Boolean, whether to display a legend.  |
| <code>legend_xy</code>      | Position for the legend, in case <code>legend</code> is TRUE.  |
| <code>pch</code>            | Graphical parameter from <code>par()</code> function.  |
| <code>main</code>           | Main title of the image  |

### Value

Heatmap of the values of the subpathways

## 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)
```

---

|       |   |
|-------|---|
| hhead | <i>Head function for SummarizedExperiment, data.frames and matrix objects</i> |
|-------|---|

---

## 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.

## Examples

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

---

|        |                       |
|--------|-----------------------|
| hidata | <i>Results object</i> |
|--------|-----------------------|

---

**Description**

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 | <i>Computes the level of activation of the subpathways for each of the samples</i> |
|----------|--|

---

**Description**

```
#@importFrom igraph
```

**Usage**

```
hipathia(
  genes_vals,
  metainfo,
  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. |
| metainfo   | 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 metainfo object to the corresponding version of the igraph package.

**Usage**

```
igraphs_upgrade(metainfo)
```

**Arguments**

```
metainfo      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_annotfuns    Loads annotations object
```

**Description**

Loads annotations object

**Usage**

```
load_annotfuns(db, species)
```

**Arguments**

```
db           Database to be used. Either "GO" or "uniprot".
species      Species of the samples.
              #@examples #load_annotfuns("GO", "hsa") #load_annotfuns("uniprot", "hsa")
```

**Value**

Annotations object

---

|             |  |
|-------------|--|
| load_annots | <i>Loads functional annotations to genes</i> |
|-------------|--|

---

**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.<br>#@examples #load_annots("GO", "hsa") |

**Value**

Functional annotations from HGNC to the selected database.

---

|                  |   |
|------------------|---|
| load_entrez_hgnc | <i>Loads table of translation from HGNC to Entrez</i> |
|------------------|---|

---

**Description**

Loads table of translation from HGNC to Entrez

**Usage**

```
load_entrez_hgnc(species)
```

**Arguments**

|         |  |
|---------|--|
| species | Species of the samples.<br>#@examples #load_entrez_hgnc("hsa") |
|---------|--|

**Value**

Table of translation from HGNC to Entrez

---

|                 |                                   |
|-----------------|-----------------------------------|
| load_gobp_frame | <i>Loads GO graph information</i> |
|-----------------|-----------------------------------|

---

**Description**

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

**Usage**

```
load_gobp_frame()
```

**Value**

GO graph information

---

|               |                       |
|---------------|-----------------------|
| load_gobp_net | <i>Loads GO graph</i> |
|---------------|-----------------------|

---

**Description**

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

**Usage**

```
load_gobp_net()
```

**Value**

GO graph

---

|          |  |
|----------|--|
| load_mgi | <i>Loads object with graph information</i> |
|----------|--|

---

**Description**

Loads object with graph information

**Usage**

```
load_mgi(species)
```

**Arguments**

|         |  |
|---------|--|
| species | Species of the samples.<br>#@examples #load_mgi("hsa") |
|---------|--|



**Value**

Graph information object

---

|               |                                   |
|---------------|-----------------------------------|
| load_pathways | <i>Loads the pathways object.</i> |
|---------------|-----------------------------------|

---

**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
pathways <- load_pathways("mmu", c("mmu03320", "mmu04024", "mmu05200"))
# Loads pathways 03320, 04024 and 05200 for mouse
```

---

|                 |   |
|-----------------|---|
| load_pseudo_mgi | <i>Loads object with pseudo graph information</i> |
|-----------------|---|

---

**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.<br>#@examples #load_pseudo_mgi("hsa", "uniprot") |

**Value**

Pseudo graph information object

---

|           |                                  |
|-----------|----------------------------------|
| load_xref | <i>Loads table of references</i> |
|-----------|----------------------------------|

---

**Description**

Loads table of references

**Usage**

```
load_xref(species)
```

**Arguments**

|         |   |
|---------|---|
| species | Species of the samples.<br>#@examples #load_xref("hsa") |
|---------|---|

**Value**

Table of references

---

|              |  |
|--------------|--|
| mgi_from_sif | <i>Create a Pathways object from SIF files</i> |
|--------------|--|

---

**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**

|                            |   |
|----------------------------|---|
| <code>sif.folder</code>    | Path to the folder in which SIF and ATT files are stored.   |
| <code>spe</code>           | Species   |
| <code>entrez_symbol</code> | 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. |
| <code>dbannot</code>       | 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`.

---

|                                |   |
|--------------------------------|---|
| <code>multiple_pca_plot</code> | <i>Plots multiple components of a PCA</i> |
|--------------------------------|---|

---

**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,
```

```

    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)

```

---

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.

**Usage**

```
node_color(
  comp,
  metainfo,
  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.   |
| metainfo | 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

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

### Arguments

|          |   |
|----------|---|
| results  | Object of results as provided by the <code>hipathia</code> function_  |
| metainfo | Object of <code>pathways_</code>  |
| group    | Character indicating the column in which the group variable is stored, in case the object provided to <code>hipathia</code> was a <code>SummarizedExperiment</code> , or a vector with the class to which each sample belongs. Samples must be ordered as in <code>results</code> .   |
| 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 <code>expdes</code> 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.  |

**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")
```

---

|                |   |
|----------------|---|
| normalize_data | <i>Normalize expression data from a SummarizedExperiment or matrix to be used in hipathia</i> |
|----------------|---|

---

**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

|                                   |  |
|-----------------------------------|--|
| <code>data</code>                 | Either a SummarizedExperiment or a matrix of gene expression.  |
| <code>sel_assay</code>            | Character or integer, indicating the assay to be normalized in the SummarizedExperiment. Default is 1.   |
| <code>by_quantiles</code>         | Boolean, whether to normalize the data by quantiles. Default is FALSE.   |
| <code>by_gene</code>              | Boolean, whether to transform the rank of each row of the matrix to [0,1]. Default is FALSE.   |
| <code>percentil</code>            | Boolean, whether to take as value the percentil of each sample in the corresponding distribution.  |
| <code>truncation_percentil</code> | 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].

### Examples

```
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 | <i>Normalize the pathway matrix by rows</i> |
|-----------------|---|

---

**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, metainfo)
```

**Arguments**

|           |  |
|-----------|--|
| path_vals | SummarizedExperiment or matrix of the pathway values |
| metainfo  | 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 | <i>Create path results table with highest significant GO ancestors</i> |
|----------------------|--|

---

**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 <code>do_wilcoxon</code> . |
| comp_go    | Wilcoxon comparison of the matrix of GO values as returned by <code>do_wilcoxon</code> .       |
| 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**

```
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**

```
data(pathways)
```

**Format**

Pathways object

**Value**

Pathways object including pathways has03320 and hsa04012.

---

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,
  metainfo,
  pathway,
  conf = 0.05,
  node_colors = NULL,
  colors = "classic"
)
```

**Arguments**

|                          |  |
|--------------------------|--|
| <code>comp</code>        | Comparison data frame as returned by the <code>do_wilcox</code> function.  |
| <code>metainfo</code>    | Pathways object.   |
| <code>pathway</code>     | Name of the pathway to be plotted.   |
| <code>conf</code>        | Level of significance of the comparison for the adjusted p-value. Default is 0.05.   |
| <code>node_colors</code> | List, named by the pathway name, including the color of each node for each pathway.  |
| <code>colors</code>      | 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**

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

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

## 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**

```
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**

```
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*

---

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

### Arguments

|                            |   |
|----------------------------|---|
| <code>fit</code>           | princomp object as returned by <code>do_pca</code>  |
| <code>group</code>         | Vector with the group to which each sample belongs. The samples must be ordered as in <code>rownames(fit\$scores)</code> . By default, all samples will be assigned to the same class.  |
| <code>sample_colors</code> | Named character vector of colors. The names of the colors must be the classes in <code>group</code> . Each sample will be assigned the color corresponding to its class, taken from the <code>group</code> vector. By default a color will be assigned automatically to each class. |
| <code>cp1</code>           | Integer, number of the component in the X-axis. Default is 1, the first component.  |
| <code>cp2</code>           | Integer, number of the component in the Y-axis. Default is 2, the second component.   |
| <code>legend</code>        | Boolean, whether to plot a legend in the plot. Default is TRUE.   |
| <code>legend_xy</code>     | Situation of the legend in the plot. Available options are: "bottomright", "bottom", "bottomleft", "left", "topleft", "top", "topright", "right" and "center".  |
| <code>cex</code>           | Graphical parameter from <code>par()</code> function.   |
| <code>pch</code>           | Graphical parameter from <code>par()</code> function.   |
| <code>mgp</code>           | Graphical parameter from <code>par()</code> 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 | <i>Plots a pathway with or without the comparison information, using the visNetwork library.</i> |
|--------|--|

---

**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". |

|         |   |
|---------|---|
| 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 | <i>Computes the level of activation of the functions related to the previously computed subpathways</i> |
|----------------|---|

---

**Description**

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

**Usage**

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

**Arguments**

|          |  |
|----------|--|
| results  | List of results as returned by the hipathia function   |
| metainfo | 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. |

|                         |  |
|-------------------------|--|
| <code>out_matrix</code> | Boolean, whether the output object should be a matrix object. Default is FALSE, returning a SummarizedExperiment object.   |
| <code>normalize</code>  | Boolean, whether to normalize the matrix of pathway values with <code>normalize_paths</code> 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**

```
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")
```

---

|                      |                       |
|----------------------|-----------------------|
| <code>results</code> | <i>Results object</i> |
|----------------------|-----------------------|

---

**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 | <i>Save results to folder</i> |
|--------------|-------------------------------|

---

**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, metainfo, output_folder = NULL, path = NULL)
```

**Arguments**

|               |   |
|---------------|---|
| results       | Results object as returned by the <code>hipathia</code> function.   |
| comp          | Comparison as returned by the <code>do_wilcoxon</code> function.  |
| metainfo      | 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**

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

---

|              |                                      |
|--------------|--------------------------------------|
| top_pathways | <i>Computes pathway significance</i> |
|--------------|--------------------------------------|

---

**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 | <i>Translation of the rownames IDs of a SummarizedExperiment to Entrez IDs.</i> |
|----------------|---|

---

**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 | <i>Translation of the rownames IDs of a matrix to Entrez IDs.</i> |
|------------------|---|

---

**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 | <i>Visualize a HiPathia report</i> |
|------------------|------------------------------------|

---

**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

**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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