

Package ‘multiDEGGs’

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Title Multi-Omic Differentially Expressed Gene-Gene Pairs

Version 1.1.3

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Description Performs multi-omic differential network

analysis by revealing differential interactions between molecular entities (genes, proteins, transcription factors, or other biomolecules) across the omic datasets provided.

For each omic dataset, a differential network is constructed where links represent statistically significant differential interactions between entities. These networks are then integrated into a comprehensive visualization using distinct colors to distinguish interactions from different omic layers. This unified display allows interactive exploration of cross-omic patterns, such as differential interactions present at both transcript and protein levels. For each link, users can access differential statistical significance metrics (p values or adjusted p values, calculated via robust or traditional linear regression with interaction term) and differential regression plots.

The methods implemented in this package are described in Sciacca et al. (2023) [<doi:10.1093/bioinformatics/btad192>](https://doi.org/10.1093/bioinformatics/btad192).

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LazyDataCompression gzip

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URL <https://github.com/elisabettasciacca/multiDEGGs/>,
<https://elisabettasciacca.github.io/multiDEGGs/>

BugReports <https://github.com/elisabettasciacca/multiDEGGs/issues>

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.predict_multiDEGGs *Predict method for multiDEGGs_filter objects*

Description

This function generates predictions by creating a dataset with single and combined predictors based on the filtering results of a multiDEGGs_filter model.

Usage

```
.predict_multiDEGGs(  
  object,  
  newdata,  
  interaction.type = "ratio",  
  sep = ":" ,  
  ...  
)
```

Arguments

object	A fitted object of class multiDEGGs_filter containing filtering results with:
keep	Character vector of variable names to keep as single predictors
pairs	Data frame or matrix with two columns specifying pairs of variables to combine
newdata	A data frame containing the new data for prediction. Must contain all variables specified in <code>object\$keep</code> and <code>object\$pairs</code> .
interaction.type	Character string specifying how to combine the paired predictors. Options are: "ratio" Combine paired predictors by dividing the first variable by the second (a/b) other Combine paired predictors by multiplying the variables (a*b) Default is "ratio".
sep	Character string used as separator when creating column names for combined predictors. Default is ":".
...	Additional arguments passed to the generic function.

Details

The function processes the filtering results in two steps:

1. Selects single predictors from newdata based on variables listed in `object$keep`
2. Adds combined predictors from paired variables in `object$pairs`

Value

A data frame containing:

- Single predictors (if any are specified in `object$keep`)
- Combined predictors based on variable pairs and interaction type

`calc_pvalues_network` *Calculate the p values for specific category network samples*

Description

Calculate the p values for specific category network samples

Usage

```
calc_pvalues_network(
  assayData,
  metadata,
  padj_method,
  categories_length,
  regression_method = "lm",
  category_network
)
```

Arguments

<code>assayData</code>	a matrix or data.frame (or list of matrices or data.frames for multi-omic analysis) containing normalised assay data. Sample IDs must be in columns and probe IDs (genes, proteins...) in rows. For multi omic analysis, it is highly recommended to use a named list of data. If unnamed, sequential names (assayData1, assayData2, etc.) will be assigned to identify each matrix or data.frame.
<code>metadata</code>	a named vector, matrix, or data.frame containing sample annotations or categories. If matrix or data.frame, each row should correspond to a sample, with columns representing different sample characteristics (e.g., treatment group, condition, time point). The colname of the sample characteristic to be used for differential analysis must be specified in <code>category_variable</code> . Rownames must match the sample IDs used in <code>assayData</code> . If named vector, each element must correspond to a sample characteristic to be used for differential analysis, and names must match sample IDs used in the colnames of <code>assayData</code> . Continuous variables are not allowed.
<code>padj_method</code>	a character string indicating the p values correction method for multiple test adjustment. It can be either one of the methods provided by the <code>p.adjust</code> function from <code>stats</code> (bonferroni, BH, hochberg, etc.) or "q.value" for Storey's q values, or "none" for unadjusted p values. When using "q.value" the <code>qvalue</code> package must be installed first.

```
categories_length
  integer number indicating the number of categories
regression_method
  whether to use robust linear modelling to calculate link p values. Options are
  'lm' (default) or 'rlm'. The lm implementation is faster and lighter.
category_network
  network table for a specific category
```

Value

a list of p values

calc_pvalues_percentile

Compute interaction p values for a single percentile value

Description

Compute interaction p values for a single percentile value

Usage

```
calc_pvalues_percentile(
  assayData,
  metadata,
  categories_length,
  category_median_list,
  padj_method,
  percentile,
  contrasts,
  regression_method,
  edges,
  sig_edges_count
)
```

Arguments

assayData	a matrix or data.frame (or list of matrices or data.frames for multi-omic analysis) containing normalised assay data. Sample IDs must be in columns and probe IDs (genes, proteins...) in rows. For multi omic analysis, it is highly recommended to use a named list of data. If unnamed, sequential names (assayData1, assayData2, etc.) will be assigned to identify each matrix or data.frame.
metadata	a named vector, matrix, or data.frame containing sample annotations or categories. If matrix or data.frame, each row should correspond to a sample, with columns representing different sample characteristics (e.g., treatment group, condition, time point). The colname of the sample characteristic to be used for differential analysis must be specified in category_variable. Rownames must

match the sample IDs used in assayData. If named vector, each element must correspond to a sample characteristic to be used for differential analysis, and names must match sample IDs used in the colnames of assayData. Continuous variables are not allowed.

categories_length	integer number indicating the number of categories
category_median_list	list of category data.frames
padj_method	a character string indicating the p values correction method for multiple test adjustment. It can be either one of the methods provided by the p.adjust function from stats (bonferroni, BH, hochberg, etc.) or "q.value" for Storey's q values, or "none" for unadjusted p values. When using "q.value" the qvalue package must be installed first.
percentile	a float number indicating the percentile to use.
contrasts	data.frame containing the categories contrasts in rows
regression_method	whether to use robust linear modelling to calculate link p values. Options are 'lm' (default) or 'rlm'. The lm implementation is faster and lighter.
edges	network of biological interactions in the form of a table of class data.frame with two columns: "from" and "to".
sig_edges_count	number of significant edges (p < 0.05)

Value

The list of float numbers of the significant pvalues for a single percentile

<code>cat_parallel</code>	<i>cat_parallel (from nestedcv)</i>
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Description

Prints using shell echo from inside mclapply when run in Rstudio

Usage

`cat_parallel(...)`

Arguments

...	to be passed to system()
-----	--------------------------

get_diffNetworks	<i>Generate multi-omic differential networks</i>
------------------	--

Description

Generate a multi-layer differential network with interaction p values

Usage

```
get_diffNetworks(  
  assayData,  
  metadata,  
  category_variable = NULL,  
  regression_method = "lm",  
  category_subset = NULL,  
  network = NULL,  
  percentile_vector = seq(0.35, 0.98, by = 0.05),  
  padj_method = "bonferroni",  
  show_progressBar = TRUE,  
  verbose = TRUE,  
  cores = parallel::detectCores()/2  
)
```

Arguments

assayData a matrix or data.frame (or list of matrices or data.frames for multi-omic analysis) containing normalised assay data. Sample IDs must be in columns and probe IDs (genes, proteins...) in rows. For multi omic analysis, it is highly recommended to use a named list of data. If unnamed, sequential names (assayData1, assayData2, etc.) will be assigned to identify each matrix or data.frame.

metadata a named vector, matrix, or data.frame containing sample annotations or categories. If matrix or data.frame, each row should correspond to a sample, with columns representing different sample characteristics (e.g., treatment group, condition, time point). The colname of the sample characteristic to be used for differential analysis must be specified in **category_variable**. Rownames must match the sample IDs used in **assayData**. If named vector, each element must correspond to a sample characteristic to be used for differential analysis, and names must match sample IDs used in the colnames of **assayData**. Continuous variables are not allowed.

category_variable when metadata is a matrix or data.frame this is the column name of **metadata** that contains the sample annotations to be used for differential analysis

regression_method whether to use robust linear modelling to calculate link p values. Options are 'lm' (default) or 'rlm'. The lm implementation is faster and lighter.

category_subset	optional character vector indicating a subset of categories from the category variable. If not specified, all categories in category_variable will be used.
network	network of biological interactions provided by the user. The network must be provided in the form of a table of class data.frame with only two columns named "from" and "to". If NULL (default) a network of 10,537 molecular interactions obtained from KEGG, miTARbase, miRecords and transmiR will be used. This has been obtained via the exportgraph function of the MITHrIL tool (Alaimo et al., 2016).
percentile_vector	a numeric vector specifying the percentiles to be used in the percolation analysis. By default, it is defined as seq(0.35, 0.98, by = 0.05), which generates a sequence of percentiles starting at 0.35, meaning that targets (genes/proteins...) whose expression value is under the 35th percentile of the whole matrix will be excluded. This threshold can be modified by specifying a different starting point for seq. For a more granular percolation analysis an higher optimisation of the algorithm, by = 0.05 can be modified in favour of lower values, but this will increase the computational time.
padj_method	a character string indicating the p values correction method for multiple test adjustment. It can be either one of the methods provided by the p.adjust function from stats (bonferroni, BH, hochberg, etc.) or "q.value" for Storey's q values, or "none" for unadjusted p values. When using "q.value" the qvalue package must be installed first.
show_progressBar	logical. Whether to display a progress bar during execution. Default is TRUE.
verbose	logical. Whether to print detailed output messages during processing. Default is TRUE
cores	number of cores to use for parallelisation.

Value

a deggs object containing differential networks incorporating p values or adjusted p values for each link.

Examples

```
# Single omic analysis:  
data("synthetic_metadata")  
data("synthetic_rnaseqData")  
deggs_object <- get_diffNetworks(assayData = synthetic_rnaseqData,  
                                  metadata = synthetic_metadata,  
                                  category_variable = "response",  
                                  regression_method = "lm",  
                                  padj_method = "bonferroni",  
                                  verbose = FALSE,  
                                  show_progressBar = FALSE,  
                                  cores = 1)  
  
# multi-omic analysis:
```

```

data("synthetic_metadata")
data("synthetic_rnaseqData")
data("synthetic_proteomicData")
data("synthetic_OlinkData")
assayData_list <- list("RNAseq" = synthetic_rnaseqData,
                       "Proteomics" = synthetic_proteomicData,
                       "Olink" = synthetic_OlinkData)
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                  metadata = synthetic_metadata,
                                  category_variable = "response",
                                  regression_method = "lm",
                                  padj_method = "bonferroni",
                                  verbose = FALSE,
                                  show_progressBar = FALSE,
                                  cores = 1)

# to use only certain categories for comparison:
# let's randomly add another level of response to the example metadata
synthetic_metadata$response <- as.character(synthetic_metadata$response)
indices <- sample(1:nrow(synthetic_metadata), 20, replace = FALSE)
synthetic_metadata$response[indices] <- "Moderate response"
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                  metadata = synthetic_metadata,
                                  category_variable = "response",
                                  category_subset = c("Responder",
                                                     "Non_responder"),
                                  regression_method = "lm",
                                  verbose = FALSE,
                                  show_progressBar = FALSE,
                                  cores = 1)

# to be more generous on the targets to be excluded, and lower the expression
# level threshold to the 25th percentile (or lower):
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                  metadata = synthetic_metadata,
                                  category_variable = "response",
                                  category_subset = c("Responder",
                                                     "Non_responder"),
                                  regression_method = "lm",
                                  percentile_vector = seq(0.25, 0.98, by = 0.05),
                                  verbose = FALSE,
                                  show_progressBar = FALSE,
                                  cores = 1)

```

get_diffNetworks_singleOmic

Generate differential networks for single omic analysis

Description

Generate differential networks for single omic analysis

Usage

```
get_diffNetworks_singleOmic(
  assayData,
  assayDataName,
  metadata,
  regression_method,
  network,
  percentile_vector,
  padj_method,
  show_progressBar,
  verbose,
  cores
)
```

Arguments

assayData	a matrix or data.frame (or list of matrices or data.frames for multi-omic analysis) containing normalised assay data. Sample IDs must be in columns and probe IDs (genes, proteins...) in rows. For multi omic analysis, it is highly recommended to use a named list of data. If unnamed, sequential names (assayData1, assayData2, etc.) will be assigned to identify each matrix or data.frame.
assayDataName	name of the assayData, to identify which omic is.
metadata	a named vector, matrix, or data.frame containing sample annotations or categories. If matrix or data.frame, each row should correspond to a sample, with columns representing different sample characteristics (e.g., treatment group, condition, time point). The colname of the sample characteristic to be used for differential analysis must be specified in category_variable. Rownames must match the sample IDs used in assayData. If named vector, each element must correspond to a sample characteristic to be used for differential analysis, and names must match sample IDs used in the colnames of assayData. Continuous variables are not allowed.
regression_method	whether to use robust linear modelling to calculate link p values. Options are 'lm' (default) or 'rlm'. The lm implementation is faster and lighter.
network	network of biological interactions provided by the user. The network must be provided in the form of a table of class data.frame with only two columns named "from" and "to". If NULL (default) a network of 10,537 molecular interactions obtained from KEGG, mirTARbase, miRecords and transmiR will be used. This has been obtained via the exportgraph function of the MITHrIL tool (Alaimo et al., 2016).
percentile_vector	a numeric vector specifying the percentiles to be used in the percolation analysis. By default, it is defined as seq(0.35, 0.98, by = 0.05), which generates a sequence of percentiles starting at 0.35, meaning that targets (genes/proteins...) whose expression value is under the 35th percentile of the whole matrix will be excluded. This threshold can be modified by specifying a different starting point for seq. For a more granular percolation analysis an higher optimisation of the

	algorithm, by = 0.05 can be modified in favour of lower values, but this will increase the computational time.
padj_method	a character string indicating the p values correction method for multiple test adjustment. It can be either one of the methods provided by the p.adjust function from stats (bonferroni, BH, hochberg, etc.) or "q.value" for Storey's q values, or "none" for unadjusted p values. When using "q.value" the qvalue package must be installed first.
show_progressBar	logical. Whether to display a progress bar during execution. Default is TRUE.
verbose	logical. Whether to print detailed output messages during processing. Default is TRUE
cores	number of cores to use for parallelisation.

Value

a list of differential networks, one per category

get_multiOmics_diffNetworks

Get a table of all significant interactions across categories

Description

Get a table of all significant interactions across categories

Usage

```
get_multiOmics_diffNetworks(deggs_object, sig_threshold = 0.05)
```

Arguments

deggs_object	an object of class deggs generated by get_diffNetworks
sig_threshold	threshold for significance. Default 0.05.

Value

a list of multilayer networks (as edge tables), one per category.

Examples

```
data("synthetic_metadata")
data("synthetic_rnaseqData")
data("synthetic_proteomicData")
data("synthetic_OlinkData")
assayData_list <- list("RNAseq" = synthetic_rnaseqData,
                      "Proteomics" = synthetic_proteomicData,
                      "Olink" = synthetic_OlinkData)
```

```
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                 metadata = synthetic_metadata,
                                 category_variable = "response",
                                 verbose = FALSE,
                                 show_progressBar = FALSE,
                                 cores = 2)
get_multiOmic_diffNetworks(deggs_object, sig_threshold = 0.05)
```

get_sig_deggs

Get a table of all the significant interactions across categories

Description

Get a table of all the significant interactions across categories

Usage

```
get_sig_deggs(deggs_object, assayDataName = 1, sig_threshold = 0.05)
```

Arguments

deggs_object an object of class deggs generated by get_diffNetworks

assayDataName name of the assayData of interest. If an unnamed list of data was given to get_diffNetworks, assayDataName here will be the number corresponding to the position of the data in the assayDataList provided before (i.e. if transcriptomic data was second in the list, a list of all its differential interactions can be obtained with assayDataName = 2, if only one data table was provided assayDataName must be 1). Default 1.

sig_threshold threshold for significance. Default 0.05.

Value

a data.frame listing all the significant differential interactions found across categories for that particular omic data. This list can also be used to substitute or integrate feature selection in machine learning models for the prediction of the categories (see vignette).

Examples

```
data("synthetic_metadata")
data("synthetic_rnaseqData")
deggs_object <- get_diffNetworks(assayData = synthetic_rnaseqData,
                                 metadata = synthetic_metadata,
                                 category_variable = "response",
                                 verbose = FALSE,
                                 show_progressBar = FALSE,
                                 cores = 2)
get_sig_deggs(deggs_object, sig_threshold = 0.05)
```

multiDEGGs_combined_filter
Combined multiDEGGs filter

Description

This function can be passed to the `modifyX` parameter of `nestcv.train` or `nestcv.glmnet` to use one of the available statistical filters (t-test, wilcoxon, etc.) in combination with multiDEGGs. Single predictors will be selected by the selected statistical filter and paired predictors will be added by multiDEGGs.

Usage

```
multiDEGGs_combined_filter(
  y,
  x,
  filter_method = "ttest",
  nfilter,
  dynamic_nfilter = TRUE,
  keep_single_genes = FALSE,
  ...
)
```

Arguments

<code>y</code>	Numeric vector or factor. Response variable (outcome), i.e. the 'metadata' named vector, as passed by <code>nestcv.train</code> or <code>nestcv.glmnet</code> .
<code>x</code>	Predictor variables, i.e. the assayData matrix with genes in columns and IDs in rows, as passed by <code>nestcv.train</code> or <code>nestcv.glmnet</code> .
<code>filter_method</code>	Character string. Statistical filtering method to be used in combination with multiDEGGs for single feature selection. Options are: "ttest", "wilcoxon", "ranger", "glmnet", "pls".
<code>nfilter</code>	Integer. Maximum number of features to select.
<code>dynamic_nfilter</code>	Logical. If TRUE <code>nfilter</code> will limit the number of features selected by the statistical filter and the feature space will be augmented by adding ALL the paired predictors found by multiDEGGs. If FALSE <code>nfilter</code> will limit the total number of predictors, with approximately half allocated to pairs and half to single genes.
<code>keep_single_genes</code>	Logical. When <code>dynamic_nfilter</code> = TRUE, determines whether to include single genes selected by multiDEGGs (i.e. the single variables included in the differential pairs) in addition to those from the statistical filter. Default is FALSE.
<code>...</code>	Additional arguments passed to the filtering functions.

Details

The function operates in two modes:

Dynamic Filtering (**dynamic_nfilter = TRUE**):

- Selects `nfilter` single genes using the specified statistical method
- Finds all significant gene pairs using `multiDEGGs`
- Total predictors = `nfilter` single genes + number of significant pairs
 - If `keep_single_genes = TRUE`, also includes single genes obtained from pairs found by `multiDEGGs`

Balanced Selection (**dynamic_nfilter = FALSE**):

- Allocates approximately half of `nfilter` to gene pairs
- Remaining slots filled with single genes from the statistical filter
- If fewer pairs are found than allocated, compensates by selecting more single genes
- Ensures consistent total number of predictors across outer folds

The statistical filtering methods include:

- `"ttest"`: Two-sample t-test for differential expression
- `"wilcoxon"`: Wilcoxon rank-sum test
- `"ranger"`: Random Forest variable importance
- `"glmnet"`: Elastic net regularization
- `"pls"`: Partial Least Squares variable importance

Value

An object of class `"multiDEGGs_filter"` containing:

<code>keep</code>	Character vector of selected single gene names
<code>pairs</code>	Data frame of selected gene pairs with interaction information

Examples

```
library(nestedcv)
data("synthetic_metadata")
data("synthetic_rnaseqData")

# fit a regularized linear model
# note that nfilter, n_outer_folds, n_inner_folds are set low to keep the
# example lightweight. Adjust these values as needed for your use case.
## Not run:
fit.glmnet <- nestedcv::nestcv.glmnet(
  y = as.numeric(synthetic_metadata$response),
  x = t(synthetic_rnaseqData),
  modifyX = "multiDEGGs_combined_filter",
  modifyX_options = list(filter_method = "ttest",
                        nfilter = 5,
```

```

dynamic_nfilter = TRUE,
keep_single_genes = FALSE),
modifyX_useY = TRUE,
n_outer_folds = 4,
n_inner_folds = 4)

summary(fit.glmnet)

## End(Not run)

# fit a random forest model
# NOTE: nfilter, n_outer_folds, n_inner_folds are set low to keep the
# example lightweight. Adjust these values as needed for your use case.
fit.rf <- nestcv::nestcv.train(
  y = synthetic_metadata$response,
  x = t(synthetic_rnaseqData),
  method = "rf",
  modifyX = "multiDEGGs_combined_filter",
  modifyX_options = list(filter_method = "ttest",
                        nfilter = 5,
                        dynamic_nfilter = TRUE,
                        keep_single_genes = FALSE),
  modifyX_useY = TRUE,
  n_outer_folds = 2,
  n_inner_folds = 2
)
fit.rf$summary

```

multiDEGGs_filter *multiDEGGs_filter*

Description

Function to be passed to the `modifyX` parameter of [nestcv.train](#) or [nestcv.glmnet](#) to allow nested feature selection and augmentation via differential network analysis with multiDEGGs.

Usage

```
multiDEGGs_filter(y, x, keep_single_genes = FALSE, nfilter = NULL)
```

Arguments

<code>y</code>	Numeric vector or factor. Response variable (outcome), i.e. the 'metadata' named vector, as passed by nestcv.train or nestcv.glmnet .
<code>x</code>	Predictor variables, i.e. the assayData matrix with genes in columns and IDs in rows, as passed by nestcv.train or nestcv.glmnet .

keep_single_genes
 Logical, default FALSE. If TRUE, the function will return unique individual genes along with significant pairs.

nfilter
 Integer. Maximum total number of predictors to return. When keep_single_genes = TRUE, this parameter limits the combined count of unique and paired predictors (i.e., $\text{length}(\text{keep_DEGGs}) + \text{nrow}(\text{pairs}) \leq \text{nfilter}$). Predictors are included from most to least significant: for each pair, both the pair itself and the new unique variables are included until the nfilter threshold is reached. When keep_single_genes = FALSE, nfilter only limits the number of pairs returned. If NULL, no filtering is applied and the total number of predictors will depend on how many significantly different interactions are detected by multiDEGGs in that fold.

Value

a list containing two types of predictors:

- single predictors (stored in the 'keep_DEGGs' vector)
- paired predictors (stored in the 'pairs' dataframe) Note that nfilter limits the maximum number of engineered features returned, however this number might be lower and will depend on how many significantly different interactions will be found in each fold by multiDEGGs.

If no significantly different interactions are found the function will print a '0' and switch to t-test for that fold.

Examples

```
library(nestedcv)
data("synthetic_metadata")
data("synthetic_rnaseqData")

# fit a regularized linear model
# Note that nfilter, n_outer_folds, n_inner_folds are set low to keep the
# example lightweight. Adjust these values as needed for your use case.
## Not run:
fit.glmnet <- nestcv.glmnet(
  y = as.numeric(synthetic_metadata$response),
  x = t(synthetic_rnaseqData),
  modifyX = "multiDEGGs_filter",
  modifyX_options = list(keep_single_genes = FALSE,
                        nfilter = 5),
  modifyX_useY = TRUE,
  n_outer_folds = 4,
  n_inner_folds = 4)

summary(fit.glmnet)

## End(Not run)

# fit a random forest model:
# note that nfilter, n_outer_folds, n_inner_folds are set low to keep the
# example lightweight. Adjust these values as needed for your use case.
```

```

fit.rf <- nestcv.train(
  y = synthetic_metadata$response,
  x = t(synthetic_rnaseqData),
  method = "rf",
  modifyX = "multiDEGGs_filter",
  modifyX_options = list(keep_single_genes = FALSE,
                        nfilter = 5),
  modifyX_useY = TRUE,
  n_outer_folds = 2,
  n_inner_folds = 2
)
fit.rf$summary

```

my_palette*Internal function for colors*

Description

This function return a color palette with the number of colors specified by n

Usage

```
my_palette(n)
```

Arguments

n	number of colors needed
---	-------------------------

Value

a vector with colors

node_boxplot*Boxplots of single nodes (genes,proteins, etc.)*

Description

This function is for internal use of View_diffnetworks

Usage

```
node_boxplot(gene, assayDataName = 1, deggs_object)
```

Arguments

gene	gene name (must be in rownames(assayData))
assayDataName	name of the assayData of interest. If an unnamed list of data was given to get_diffNetworks, the assayDataName here will be the number indicating the position of the data in the assayDataList provided before (i.e. if the user wants to plot a differential interaction observed in the transcriptomic data, which was second in the list, then assayDataName must be 2, if only one data table was provided assayDataName must be 1). Default 1.
deggs_object	an object of class deggs generated by get_diffNetworks

Value

the boxplot

plot_regressions *Plot differential regressions for a link*

Description

Plot differential regressions for any target-target pair in an omic dataset

Usage

```
plot_regressions(
  deggs_object,
  assayDataName = 1,
  gene_A,
  gene_B,
  title = NULL,
  legend_position = "topright"
)
```

Arguments

deggs_object	an object of class deggs generated by get_diffNetworks
assayDataName	name of the assayData of interest. If an unnamed list of data was given to get_diffNetworks, the assayDataName here will be the number indicating the position of the data in the assayDataList provided before (i.e. if the user wants to plot a differential interaction observed in the transcriptomic data, which was second in the list, then assayDataName must be 2, if only one data table was provided assayDataName must be 1). Default 1.
gene_A	character. Name of the first target (gene, protein, metabolite, etc.)
gene_B	character. Name of the second target (gene, protein, metabolite, etc.)
title	plot title. If NULL (default), the name of the assayData will be used. Use empty character "" for no title.

```
legend_position
position of the legend in the plot. It can be specified by keyword or in any
parameter accepted by xy.coords (defalut "topright")
```

Value

base graphics plot showing differential regressions across categories. The p value of the interaction term of gene A ~ gene B * category is reported on top.

Examples

```
data("synthetic_metadata")
data("synthetic_rnaseqData")
data("synthetic_proteomicData")
data("synthetic_OlinkData")
assayData_list <- list("RNAseq" = synthetic_rnaseqData,
                      "Proteomics" = synthetic_proteomicData,
                      "Olink" = synthetic_OlinkData)
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                  metadata = synthetic_metadata,
                                  category_variable = "response",
                                  regression_method = "lm",
                                  padj_method = "bonferroni",
                                  verbose = FALSE,
                                  show_progressBar = FALSE,
                                  cores = 1)
plot_regressions(deggs_object,
                  assayDataName = "RNAseq",
                  gene_A = "MTOR",
                  gene_B = "AKT2",
                  legend_position = "bottomright")
```

predict.multiDEGGs_filter

Wrapper of .predict_multiDEGGs for multiDEGGs_filter()

Description

This function generates predictions by creating a dataset with single and combined predictors based on the filtering results of a multiDEGGs_filter model.

Usage

```
## S3 method for class 'multiDEGGs_filter'
predict(object, newdata, interaction.type = "ratio", sep = ":", ...)
```

Arguments

object	A fitted object of class <code>multiDEGGs_filter</code> containing filtering results with:
keep	Character vector of variable names to keep as single predictors
pairs	Data frame or matrix with two columns specifying pairs of variables to combine
newdata	A data frame containing the new data for prediction. Must contain all variables specified in <code>object\$keep</code> and <code>object\$pairs</code> .
interaction.type	Character string specifying how to combine the paired predictors. Options are: "ratio" Combine paired predictors by dividing the first variable by the second (a/b) other Combine paired predictors by multiplying the variables (a*b) Default is "ratio".
sep	Character string used as separator when creating column names for combined predictors. Default is ":".
...	Additional arguments passed to the generic function.

Details

The function processes the filtering results in two steps:

1. Selects single predictors from `newdata` based on variables listed in `object$keep`
2. Adds combined predictors from paired variables in `object$pairs`

Value

A data frame containing:

- Single predictors (if any are specified in `object$keep`)
- Combined predictors based on variable pairs and interaction type

`predict.multiDEGGs_filter_combined`

Wrapper of .predict_multiDEGGs for multiDEGGs_filter_combined()

Description

This function generates predictions by creating a dataset with single and combined predictors based on the filtering results of a `multiDEGGs_filter` model.

Usage

```
## S3 method for class 'multiDEGGs_filter_combined'
predict(object, newdata, interaction.type = "ratio", sep = ":", ...)
```

Arguments

object	A fitted object of class <code>multiDEGGs_filter</code> containing filtering results with:
	keep Character vector of variable names to keep as single predictors
	pairs Data frame or matrix with two columns specifying pairs of variables to combine
newdata	A data frame containing the new data for prediction. Must contain all variables specified in <code>object\$keep</code> and <code>object\$pairs</code> .
interaction.type	Character string specifying how to combine the paired predictors. Options are: "ratio" Combine paired predictors by dividing the first variable by the second (a/b) other Combine paired predictors by multiplying the variables (a*b) Default is "ratio".
sep	Character string used as separator when creating column names for combined predictors. Default is ":".
...	Additional arguments passed to the generic function.

Details

The function processes the filtering results in two steps:

1. Selects single predictors from `newdata` based on variables listed in `object$keep`
2. Adds combined predictors from paired variables in `object$pairs`

Value

A data frame containing:

- Single predictors (if any are specified in `object$keep`)
- Combined predictors based on variable pairs and interaction type

`synthetic_metadata` *Synthetic clinical data*

Description

A dataset containing sample clinical data for 100 patients with 40% response rate

Format

A data frame with 100 rows and 4 columns (IDs are in rownames):

patient_id IDs matching the IDs used in the colnames of the assay data matrix/matrices.
age A column to simulate age of patients. Not used.
gender A column to simulate gender of patients. Not used.
response The response outcome, to be used for differential analysis

synthetic_OlinkData *Synthetic RNA-seq count data*

Description

Synthetic RNA-seq data after log2 normalisation

Format

A data frame with xx rows (proteins) xx columns (patients IDs).

synthetic_proteomicData
Synthetic RNA-seq count data

Description

Synthetic RNA-seq data after log2 normalisation

Format

A data frame with xx rows (proteins) xx columns (patients IDs).

synthetic_rnaseqData *Synthetic RNA-seq count data*

Description

Synthetic RNA-seq data after log2 normalisation

Format

A data frame with xx rows (genes) xx columns (patients IDs, matching the metadata rownames).

tidy_metadata	<i>Tidying up of metadata. Samples belonging to undesired categories (if specified) will be removed as well as categories with less than five samples, and NAs.</i>
---------------	---

Description

Tidying up of metadata. Samples belonging to undesired categories (if specified) will be removed as well as categories with less than five samples, and NAs.

Usage

```
tidy_metadata(  
  category_subset = NULL,  
  metadata,  
  category_variable = NULL,  
  verbose = FALSE  
)
```

Arguments

category_subset	optional character vector indicating which categories are used for comparison. If not specified, all categories in category_variable will be used.
metadata	a named vector, matrix, or data.frame containing sample annotations or categories. If matrix or data.frame, each row should correspond to a sample, with columns representing different sample characteristics (e.g., treatment group, condition, time point). The colname of the sample characteristic to be used for differential analysis must be specified in category_variable. Rownames must match the sample IDs used in assayData. If named vector, each element must correspond to a sample characteristic to be used for differential analysis, and names must match sample IDs used in the colnames of assayData. Continuous variables are not allowed.
category_variable	column name in metadata (if data.frame or matrix) or NULL if metadata is already a named vector containing category information.
verbose	Logical. Whether to print detailed output messages during processing. Default is FALSE.

Value

a tidy named factor vector of sample annotations.

View_diffNetworks *Interactive visualisation of differential networks*

Description

Explore differential networks and interactively select regression and box plots

Usage

```
View_diffNetworks(deggs_object, legend.arrow.width = 0.35, stepY_legend = 55)
```

Arguments

deggs_object	an object of class deggs generated by get_diffNetworks
legend.arrow.width	width of the arrow used in the network legend. Default is 0.35. As the number of assayData matrices increases this parameter must be accordingly increased to avoid graphical errors in the legend.
stepY_legend	vertical space between legend arrows. It is used together with legend.arrow.width to adjust the legend space in case of graphical errors. Default is 55.

Value

a shiny interface showing networks with selectable nodes and links

Examples

```
data("synthetic_metadata")
data("synthetic_rnaseqData")
data("synthetic_proteomicData")
data("synthetic_OlinkData")
assayData_list <- list("RNAseq" = synthetic_rnaseqData,
                      "Proteomics" = synthetic_proteomicData,
                      "Olink" = synthetic_OlinkData)
deggs_object <- get_diffNetworks(assayData = assayData_list,
                                  metadata = synthetic_metadata,
                                  category_variable = "response",
                                  regression_method = "lm",
                                  verbose = FALSE,
                                  show_progressBar = FALSE,
                                  cores = 1)
# the below function runs a shiny app, so can't be run during R CMD check
if(interactive()){
  View_diffNetworks(deggs_object)
}
```

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