Package 'CEMiTool'

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Title Co-expression Modules identification Tool

Version 1.4.2

Description The CEMiTool package unifies the discovery and the analysis of coexpression gene modules in a fully automatic manner, while providing a user-friendly html report with high quality graphs. Our tool evaluates if modules contain genes that are over-represented by specific pathways or that are altered in a specific sample group. Additionally, CEMiTool is able to integrate transcriptomic data with interactome information, identifying the potential hubs on each network.

Depends R (>= 3.4)

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R topics documented:

`adj_data` *Get or set adjacency matrix value*

Description

This function takes a `CEMiTool` object containing expression values and returns a CEMiTool object with an adjacency matrix in the adjacency slot.

Usage

```
adj_data(cem, ...)

## S4 method for signature 'CEMiTool'
adj_data(cem)

adj_data(cem) <- value

## S4 replacement method for signature 'CEMiTool'
adj_data(cem) <- value
```

Arguments

`cem`	Object of class `CEMiTool`
`...`	Optional parameters.
`value`	Object of class `matrix` containing adjacency data. Only used for setting adjacency values to CEMiTool object.

Value

Object of class `matrix` with adjacency values or object of class `CEMiTool`.

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Calculate adjacency matrix with example beta value 8
cem <- get_adj(cem, beta=8)
# Return adjacency matrix
adj <- adj_data(cem)
# Check result
adj[1:5, 1:5]
# Set adjacency matrix to CEMiTool object
adj_data(cem) <- adj
```

cem *CEMiTool Object*

Description

This object can be used as input for CEMiTool functions. Data used are from `expr` and `sample_annot`.

Usage

```
data(cem)
```

Format

An object of class `CEMiTool`

Examples

```
# Get example CEMiTool object
data(cem)
cem
```

cemitool *Full gene co-expression analysis*

Description

Defines co-expression modules and runs several different analyses.

Usage

```
cemitool(expr, annot, gmt, interactions, filter = TRUE, filter_pval = 0.1,
  apply_vst = FALSE, n_genes, eps = 0.1, cor_method = c("pearson",
  "spearman"), cor_function = "cor", network_type = "unsigned",
  tom_type = "signed", set_beta = NULL, force_beta = FALSE,
  sample_name_column = "SampleName", class_column = "Class",
  merge_similar = TRUE, rank_method = "mean", ora_pval = 0.05,
  gsea_scale = TRUE, gsea_min_size = 15, gsea_max_size = 500,
  min_ngen = 30, diss_thresh = 0.8, plot = TRUE, order_by_class = TRUE,
  center_func = "mean", directed = FALSE, verbose = FALSE)
```

Arguments

`expr`	Gene expression `data.frame`.
`annot`	Sample annotation `data.frame`.
`gmt`	A data.frame containing two columns, one with pathways and one with genes
`interactions`	A data.frame containing two columns with gene names.
`filter`	Logical. If TRUE, will filter expression data.
`filter_pval`	P-value threshold for filtering.Default `0.1`.

apply_vst	Logical. If TRUE, will apply Variance Stabilizing Transform before filtering genes. Currently ignored if parameter filter is FALSE.
n_genes	Number of genes left after filtering.
eps	A value for accepted R-squared interval between subsequent beta values. Default is 0.1.
cor_method	A character string indicating which correlation coefficient is to be computed. One of "pearson" or "spearman". Default is "pearson".
cor_function	A character string indicating the correlation function to be used. Supported functions are currently 'cor' and 'bicor'. Default is "cor"
network_type	A character string indicating if network type should be computed as "signed" or "unsigned". Default is "unsigned"
tom_type	A character string indicating if the TOM type should be computed as "signed" or "unsigned". Default is "signed"
set_beta	A value to override the automatically selected beta value. Default is NULL.
force_beta	Whether or not to automatically force a beta value based on number of samples. Default is FALSE.
sample_name_column	A character string indicating the sample column name of the annotation table.
class_column	A character string indicating the class column name of the annotation table.
merge_similar	Logical. If TRUE, merge similar modules.
rank_method	Character string indicating how to rank genes. Either "mean" (the default) or "median".
ora_pval	P-value for overrepresentation analysis. Default 0.05.
gsea_scale	If TRUE, apply z-score transformation for GSEA analysis. Default is TRUE
gsea_min_size	Minimum size of gene sets for GSEA analysis. Default is 15
gsea_max_size	Maximum size of gene sets for GSEA analysis. Default is 500
min_ngen	Minimal number of genes per submodule. Default 30.
diss_thresh	Module merging correlation threshold for eigengene similarity. Default 0.8.
plot	Logical. If TRUE, plots all figures.
order_by_class	Logical. If TRUE, samples in profile plot are ordered by the groups defined by the class_column slot in the sample annotation file. Ignored if there is no sample_annotation file. Default TRUE.
center_func	Character string indicating the centrality measure to show in the plot. Either 'mean' (the default) or 'median'.
directed	Logical. If TRUE, the igraph objects in interactions slot will be directed.
verbose	Logical. If TRUE, reports analysis steps.

Value

Object of class CEMiTool

Examples

```
## Not run:
# Get example expression data
data(expr0)
# Run CEMiTool analyses
cem <- cemitool(expr=expr0)
# Run CEMiTool applying Variance Stabilizing Transformation to data
cem <- cemitool(expr=expr0, apply_vst=TRUE)
# Run CEMiTool with additional processing messages
cem <- cemitool(expr=expr0, verbose=TRUE)

# Run full CEMiTool analysis
## Get example sample annotation data
data(sample_annot)
## Read example pathways file
gmt_fname <- system.file("extdata", "pathways.gmt", package = "CEMiTool")
gmt_in <- read_gmt(gmt_fname)
## Get example interactions file
int_df <- read.delim(system.file("extdata", "interactions.tsv", package = "CEMiTool"))
## Run CEMiTool
cem <- cemitool(expr=expr0, annot=sample_annot, gmt=gmt_in,
    interactions=int_df, verbose=TRUE, plot=TRUE)

# Create report as html file
generate_report(cem, directory = "./Report", output_format="html_document")

# Write analysis results into files
write_files(cem, directory="./Tables", force=TRUE)

# Save all plots
save_plots(cem, "all", directory="./Plots")

## End(Not run)
```

`CEMiTool-class` *An S4 class to represent the CEMiTool analysis.*

Description

An S4 class to represent the CEMiTool analysis.

Slots

`expression` Gene expression `data.frame`.

`sample_annotation` Sample annotation `data.frame`.

`fit_indices` `data.frame` containing scale-free model fit, soft-threshold and network parameters.

`selected_genes` Character `vector` containing the names of genes selected for analysis

`module` Genes in modules information `data.frame`.

`enrichment` `list` with modules enrichment results for sample classes.

`ora` Over-representation analysis results `data.frame`.

`interactions` `list` containing gene interactions present in modules.

`interaction_plot` list of ggplot graphs with module gene interactions.

`profile_plot` list of ggplot graphs with gene expression profile per module.

`enrichment_plot` ggplot graph for enrichment analysis results.

`beta_r2_plot` ggplot graph with scale-free topology fit results for each soft-threshold.

`mean_k_plot` ggplot graph with mean network connectivity.

`barplot_ora` list of ggplot graphs with over-representation analysis results per module.

`sample_tree_plot` gtable containing sample dendrogram with class labels and clinical data (if available in sample_annotation(cem)).

`mean_var_plot` Mean x variance scatterplot.

`hist_plot` Expression histogram.

`qq_plot` Quantile-quantile plot.

`sample_name_column` character string containing the name of the column with sample names in the annotation file.

`class_column` character string containing the name of the column with class names in the annotation file.

`mod_colors` character `vector` containing colors associated with each network module.

`parameters` `list` containing analysis parameters.

`adjacency` `matrix` containing gene adjacency values based on correlation

Examples

```
# Get example expression data
data(expr0)
# Initialize CEMiTool object with expression
cem <- new("CEMiTool", expression=expr0)
```

`cem_overlap` *Integrates CEMiTool analyses*

Description

Returns the occurrence of edges between different analyses

Usage

```
cem_overlap(..., analyses_list = NULL, fraction = 1)
```

Arguments

`...`	Objects of class `CEMiTool`, data.frames or character string containing the path to a file with genes and modules.
`analyses_list`	List of objects of class `CEMiTool`, data.frames or character strings containing the path to files with genes and modules.
`fraction`	The fraction of objects in which an edge pair must be present to be selected (default = 1, accepts values from 0-1)

Details

The method assumes that all genes inside each module are connected to every other gene from the same module.

Value

Object of class `data.frame` containing edgelist describing common edges between the networks defined in module slots from the input objects

Examples

```
## Not run:
# Run cemitool twice on expr dataset. In each time, one sample will be removed
data(expr0)
set.seed(10)
dset1 <- expr0[,-sample(1:ncol(expr0), 1)]
dset2 <- expr0[,-sample(1:ncol(expr0), 1)]
cem1 <- cemitool(dset1)
cem2 <- cemitool(dset2)
cemoverlap_df <- cem_overlap(cem1, cem2)
# Can also be run with a list: cemoverlap_df <- cemoverlap(list(cem1, cem2))

# Different types of objects can be combined as well, and invalid objects will
be removed, with a warning
cemoverlap_df <- cem_overlap(cem1, cem2, module_genes(cem), NA, 1, NULL)

## End(Not run)
```

`diagnostic_report` *Diagnostic report*

Description

Creates report for identifying potential problems with data.

Usage

```
diagnostic_report(cem, ...)

## S4 method for signature 'CEMiTool'
diagnostic_report(cem, title = "Diagnostics",
  directory = "./Reports/Diagnostics", force = FALSE, ...)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	parameters to rmarkdown::render
`title`	Character string with the title of the report.
`directory`	Directory name for results.
`force`	If the directory exists, execution will not stop.

Value

An HTML file with an interactive diagnostic report.

---

expr0 *Yellow Fever gene expression data from GEO study GSE13485*

Description

Modified data from a yellow fever vaccination study by Querec et al, 2009. In order to reduce package size, only the 4000 genes with the highest variance were selected for this dataset.

Usage

```
data(expr0)
```

Format

An object of class `data.frame`

Source

GEO

References

Querec TD, Akondy RS, Lee EK, Cao W et al. Systems biology approach predicts immunogenicity of the yellow fever vaccine in humans. Nat Immunol 2009 Jan;10(1):116-25. PMID: 19029902 PubMed

Examples

```
data(expr0)
# Run CEMiTool analysis
## Not run: cemitool(expr0)
```

---

expr_data *Retrieve and set expression attribute*

Description

Retrieve and set expression attribute

Usage

```
expr_data(cem, ...)

## S4 method for signature 'CEMiTool'
expr_data(cem, filtered = TRUE)

expr_data(cem) <- value

## S4 replacement method for signature 'CEMiTool'
expr_data(cem) <- value
```

Arguments

cem	Object of class CEMiTool
...	Optional parameters.
filtered	logical. If TRUE retrieves filtered expression data
value	Object of class data.frame with gene expression data

Value

Object of class data.frame with gene expression data

Examples

```
# Initialize an empty CEMiTool object
cem <- new_cem()
# Get example expression data
data(expr0)
# Add expression file to CEMiTool object
expr_data(cem) <- expr0
# Check expression file
head(expr_data(cem))
```

---

filter_expr *Filter gene expression table*

Description

Filter gene expression table

Usage

```
filter_expr(cem, ...)

## S4 method for signature 'CEMiTool'
filter_expr(cem, filter_pval = 0.1, n_genes,
  pct = 0.75, apply_vst = FALSE)
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
filter_pval	P-value cutoff for gene selection.
n_genes	Number of genes to be selected.
pct	Percentage of most expressed genes to keep (before variance filter).
apply_vst	Logical. If TRUE, will apply variance stabilizing transform before filtering data.

Value

Object of class CEMiTool with selected genes

Examples

```
# Get example expression data
data(expr0)
# Initialize CEMiTool object with expression
cem <- new_cem(expr0)
# Filter genes
cem1 <- filter_expr(cem)
# Check selected genes
head(expr_data(cem1))
# Filter genes and apply variance stabilizing transformation
cem2 <- filter_expr(cem, apply_vst=TRUE)
# Check results
head(expr_data(cem2))
```

`find_modules` *Co-expression modules definition*

Description

Defines co-expression modules

Usage

```
find_modules(cem, ...)

## S4 method for signature 'CEMiTool'
find_modules(cem, cor_method = c("pearson", "spearman"),
  cor_function = "cor", eps = 0.1, set_beta = NULL, force_beta = FALSE,
  min_ngen = 20, merge_similar = TRUE, network_type = "unsigned",
  tom_type = "signed", diss_thresh = 0.8, verbose = FALSE)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`cor_method`	A character string indicating which correlation coefficient is to be computed. Default `"pearson"`
`cor_function`	A character string indicating the correlation function to be used. Default `'cor'`.
`eps`	A value for accepted R-squared interval between subsequent beta values. Default is 0.1.
`set_beta`	A value to override the automatically selected beta value. Default is NULL.
`force_beta`	Whether or not to automatically force a beta value based on number of samples. Default is FALSE.
`min_ngen`	Minimal number of genes per submodule. Default `20`.
`merge_similar`	Logical. If `TRUE`, (the default) merge similar modules.
`network_type`	A character string indicating to use either "unsigned" (default) or "signed" networks. Default `"unsigned"`

tom_type	A character string indicating to use either "unsigned" or "signed" (default) TOM similarity measure.
diss_thresh	Module merging correlation threshold for eigengene similarity. Default 0.8.
verbose	Logical. If TRUE, reports analysis steps. Default FALSE

Value

Object of class CEMiTool

Examples

```
# Get example expression data
data(expr0)
# Initialize CEMiTool object with expression
cem <- new_cem(expr0)
# Filter data
cem <- filter_expr(cem)
# Define network modules
cem <- find_modules(cem)
# Check results
head(module_genes(cem))
```

---

fit_data *Retrieve scale-free model fit data*

Description

Retrieve scale-free model fit data

Usage

```
fit_data(cem)

## S4 method for signature 'CEMiTool'
fit_data(cem)
```

Arguments

cem	Object of class CEMiTool

Value

Object of class data.frame

Examples

```
# Get example CEMiTool object
data(cem)
# Get modules and beta data
cem <- find_modules(cem)
# Get fit data
fit_data(cem)
```

`generate_report` *CEMiTool report*

Description

Creates report for CEMiTool results

Usage

```
generate_report(cem, ...)

## S4 method for signature 'CEMiTool'
generate_report(cem, max_rows_ora = 50,
  title = "Report", directory = "./Reports/Report", force = FALSE, ...)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	parameters to rmarkdown::render
`max_rows_ora`	maximum number of rows in Over Representation Analysis table results
`title`	Character string with the title of the report.
`directory`	Directory name for results.
`force`	If the directory exists, execution will not stop.

Value

An HTML file with an interactive report of CEMiTool analyses.

Examples

```
## Not run:
# Get example CEMiTool object
data(cem)
generate_report(cem, output_format=c("pdf_document", "html_document"))

## End(Not run)
```

`geom_qq_line` *Geom qq*

Description

Geom qq

‘geom_qq‘ and ‘stat_qq‘ produce quantile-quantile plots. ‘geom_qq_line‘ and ‘stat_qq_line‘ compute the slope and intercept of the line connecting the points at specified quartiles of the theoretical and sample distributions. These functions have been taken from the development version of ggplot2 and will be removed as soon as they are implemented in the release version.

Usage

```
geom_qq_line(mapping = NULL, data = NULL, geom = "path",
  position = "identity", ..., distribution = stats::qnorm,
  dparams = list(), line.p = c(0.25, 0.75), fullrange = FALSE,
  na.rm = FALSE, show.legend = NA, inherit.aes = TRUE)

stat_qq_line(mapping = NULL, data = NULL, geom = "path",
  position = "identity", ..., distribution = stats::qnorm,
  dparams = list(), line.p = c(0.25, 0.75), fullrange = FALSE,
  na.rm = FALSE, show.legend = NA, inherit.aes = TRUE)

geom_qq(mapping = NULL, data = NULL, geom = "point",
  position = "identity", ..., distribution = stats::qnorm,
  dparams = list(), na.rm = FALSE, show.legend = NA, inherit.aes = TRUE)

stat_qq(mapping = NULL, data = NULL, geom = "point",
  position = "identity", ..., distribution = stats::qnorm,
  dparams = list(), na.rm = FALSE, show.legend = NA, inherit.aes = TRUE)
```

Arguments

mapping	Parameter to ggplot
data	Parameter to ggplot
geom	Parameter to ggplot
position	Parameter to ggplot
...	Parameter to ggplot
distribution	Distribution function to use, if x not specified
dparams	Additional parameters passed on to ‘distribution‘ function.
line.p	Vector of quantiles to use when fitting the Q-Q line, defaults defaults to ‘c(.25, .75)‘.
fullrange	Should the q-q line span the full range of the plot, or just the data
na.rm	Parameter to ggplot
show.legend	Parameter to ggplot
inherit.aes	Parameter to ggplot

Value

ggplot

Examples

```
## Not run:
df <- data.frame(y = rt(200, df = 5))
p <- ggplot(df, aes(sample = y))
p + stat_qq() + stat_qq_line()

# Use fitdistr from MASS to estimate distribution params
params <- as.list(MASS::fitdistr(df$y, "t")$estimate)
ggplot(df, aes(sample = y)) +
  stat_qq(distribution = qt, dparams = params["df"]) +
```

```
  stat_qq_line(distribution = qt, dparams = params["df"])

# Using to explore the distribution of a variable
ggplot(mtcars, aes(sample = mpg)) +
  stat_qq() +
  stat_qq_line()
ggplot(mtcars, aes(sample = mpg, colour = factor(cyl))) +
  stat_qq() +
  stat_qq_line()

## End(Not run)
```

`get_adj` *Calculate adjacency matrix*

Description

This function takes a `CEMiTool` object and returns an adjacency matrix.

Usage

```
get_adj(cem, ...)

## S4 method for signature 'CEMiTool'
get_adj(cem, beta, network_type = "unsigned",
  cor_function = "cor", cor_method = "pearson")
```

Arguments

`cem`	Object of class `CEMiTool`
`...`	Optional parameters.
`beta`	Selected soft-threshold value
`network_type`	A character string indicating to use either "unsigned" (default) or "signed" networks. Default `"unsigned"`.
`cor_function`	A character string indicating the correlation function to be used. Default `'cor'`.
`cor_method`	A character string indicating which correlation coefficient is to be computed. Default `"pearson"`.

Value

Object of class `CEMiTool` with adjacency data

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Calculate adjacency matrix with example beta value 8
cem <- get_adj(cem, beta=8)
```

```
# Check results
adj <- adj_data(cem)
adj[1:5, 1:5]
```

`get_beta_data` *Soft-threshold beta data*

Description

This function takes the input parameters from find_modules and calculates the WGCNA soft-threshold parameters and returns them.

Usage

```
get_beta_data(cem, ...)

## S4 method for signature 'CEMiTool'
get_beta_data(cem, network_type = "unsigned",
  cor_function = "cor", cor_method = "pearson", verbose = FALSE)
```

Arguments

`cem`	A CEMiTool object containing expression data
`...`	Optional parameters.
`network_type`	A character string indicating to use either "unsigned" (default) or "signed" networks. Default `"unsigned"`.
`cor_function`	A character string indicating the correlation function to be used. Default `'cor'`.
`cor_method`	A character string indicating which correlation coefficient is to be computed. Default `"pearson"`
`verbose`	Logical. If `TRUE`, reports analysis steps. Default `FALSE`

Value

A list containing the soft-threshold selected by WGCNA and scale-free model parameters

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Get beta data
beta_data <- get_beta_data(cem)
```

get_cemitool_r2_beta *Calculate CEMiTool beta and R2 values*

Description

This function takes a CEMiTool object with beta data and returns a vector containing the chosen beta and corresponding R squared value.

Usage

```
get_cemitool_r2_beta(cem, ...)

## S4 method for signature 'CEMiTool'
get_cemitool_r2_beta(cem, eps = 0.1)
```

Arguments

cem	A CEMiTool object containing the fit_indices slot
...	Optional parameters.
eps	A value indicating the accepted interval between successive values of R squared to use to calculate the selected beta. Default: 0.1.

Value

A vector containing R squared value and the chosen beta parameter.

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Get modules and beta data
cem <- find_modules(cem)
# Get CEMiTool R2 and beta values
get_cemitool_r2_beta(cem)
```

get_connectivity *Calculate network connectivity*

Description

This function takes a CEMiTool object and returns the network connectivity.

Usage

```
get_connectivity(cem, ...)

## S4 method for signature 'CEMiTool'
get_connectivity(cem, beta)
```

Arguments

cem	Object of class CEMiTool containing the fit_indices slot
...	Optional parameters.
beta	A soft-thresholding value to be used for the network.

Value

The value of the network's connectivity.

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Get modules and beta data
cem <- find_modules(cem)
# Get network connectivity with example beta value 8
get_connectivity(cem, beta=8)
```

---

get_hubs *Get hubs*

Description

Returns n genes in each module with high connectivity.

Usage

```
get_hubs(cem, ...)

## S4 method for signature 'CEMiTool'
get_hubs(cem, n = 5)
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
n	Number of genes to return in each module (default: 5).

Value

A `list` containing hub genes.

Examples

```
# Get example CEMiTool object
data(cem)
# Get module hubs
hubs <- get_hubs(cem, n=10)
```

`get_merged_mods` *Merge similar modules*

Description

This function takes a CEMiTool object with expression and a vector of numeric labels to merge similar modules.

Usage

```
get_merged_mods(cem, ...)

## S4 method for signature 'CEMiTool'
get_merged_mods(cem, mods, diss_thresh = 0.8,
  verbose = FALSE)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`mods`	A vector containing numeric labels for each module gene
`diss_thresh`	A threshold of dissimilarity for modules. Default is 0.8.
`verbose`	Logical. If `TRUE`, reports analysis steps. Default `FALSE`

Value

Numeric labels assigning genes to modules.

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Calculate adjacency matrix with example beta value 8
cem <- get_adj(cem, beta=8)
# Get modules
mods <- get_mods(cem)
```

```
# Merge similar modules
merged_mods <- get_merged_mods(cem, mods)
```

`get_mods` *Calculate co-expression modules*

Description

This function takes a `CEMiTool` object containing an adjacency matrix together with the given network parameters, and returns the given co-expression modules.

Usage

```
get_mods(cem, ...)

## S4 method for signature 'CEMiTool'
get_mods(cem, cor_function = "cor",
  cor_method = "pearson", tom_type = "signed", min_ngen = 20)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`cor_function`	A character string indicating the correlation function to be used. Default `'cor'`.
`cor_method`	A character string indicating which correlation coefficient is to be computed. Default `"pearson"`.
`tom_type`	A character string indicating to use either "unsigned" or "signed" (default) TOM similarity measure.
`min_ngen`	Minimal number of genes per module (Default: 20).

Value

Numeric labels assigning genes to modules.

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Calculate adjacency matrix with example beta value 8
cem <- get_adj(cem, beta=8)
# Get module labels
mods <- get_mods(cem)
```

get_phi *Calculate phi*

Description

This function takes a CEMiTool object and returns the phi parameter.

Usage

```
get_phi(cem, ...)

## S4 method for signature 'CEMiTool'
get_phi(cem)
```

Arguments

cem	A CEMiTool object containing the fit_indices slot
...	Optional parameters.

Value

The phi parameter

Examples

```
# Get example expression data
data(expr0)
# Initialize new CEMiTool object with expression data
cem <- new_cem(expr0)
# Filter expression data
cem <- filter_expr(cem)
# Get modules and beta data
cem <- find_modules(cem)
# Get phi
get_phi(cem)
```

gsea_data *Retrieve Gene Set Enrichment Analysis (GSEA) results*

Description

Retrieve Gene Set Enrichment Analysis (GSEA) results

Usage

```
gsea_data(cem)

## S4 method for signature 'CEMiTool'
gsea_data(cem)
```

Arguments

cem	Object of class CEMiTool

Value

Object of class list with GSEA data

Examples

```
# Get example CEMiTool object
data(cem)
# Look at example annotation file
sample_annotation(cem)
# Run GSEA on network modules
cem <- mod_gsea(cem)
# Check results
gsea_data(cem)
```

---

interactions_data *Retrieve and set interaction data to CEMiTool object*

Description

Retrieve and set interaction data to CEMiTool object

Usage

```
interactions_data(cem, ...)

## S4 method for signature 'CEMiTool'
interactions_data(cem)

interactions_data(cem) <- value

## S4 replacement method for signature 'CEMiTool'
interactions_data(cem) <- value
```

Arguments

cem	Object of class CEMiTool.
...	parameters for igraph::graph_from_data_frame
value	a data.frame or matrix containing two columns

Value

Object of class CEMiTool

Examples

```
# Get example CEMiTool object
data(cem)
# Read example interactions data
int_df <- read.delim(system.file("extdata", "interactions.tsv",
    package = "CEMiTool"))
# Insert interactions data
interactions_data(cem) <- int_df
# Check interactions data
interactions_data(cem)
```

`module_genes` *Get the module genes in a CEMiTool object*

Description

Get the module genes in a CEMiTool object

Usage

```
module_genes(cem, module = NULL)

## S4 method for signature 'CEMiTool'
module_genes(cem, module = NULL)
```

Arguments

`cem`	Object of class `CEMiTool`
`module`	A character string with the name of the module of which genes are to be returned. Defaults to `NULL`, which returns the full list of genes and modules.

Value

Object of class `data.frame` containing genes and their respective module

Examples

```
# Get example CEMiTool object
data(cem)
# Get the module genes
module_genes(cem)
# Get genes for module M1
module_genes(cem, module="M1")
```

mod_colors *Retrieve and set mod_colors attribute*

Description

Retrieve and set mod_colors attribute

Usage

```
mod_colors(cem)

## S4 method for signature 'CEMiTool'
mod_colors(cem)

mod_colors(cem) <- value

## S4 replacement method for signature 'CEMiTool,character'
mod_colors(cem) <- value
```

Arguments

cem	Object of class CEMiTool
value	a character vector containing colors for each module. Names should match with module names

Value

A vector with color names.

Examples

```
# Get example CEMiTool object
data(cem)
# See module colors
mod_colors(cem)
```

mod_gsea *Module Gene Set Enrichment Analysis*

Description

Perfoms Gene Set Enrichment Analysis (GSEA) for each co-expression module found.

Usage

```
mod_gsea(cem, ...)

## S4 method for signature 'CEMiTool'
mod_gsea(cem, gsea_scale = TRUE, rank_method = "mean",
  gsea_min_size = 15, gsea_max_size = 500, verbose = FALSE)
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
gsea_scale	If TRUE, transform data using z-score transformation. Default: TRUE
rank_method	Character string indicating how to rank genes. Either "mean" (the default) or "median".
gsea_min_size	Minimum gene set size
gsea_max_size	Maximum gene set size
verbose	logical. Report analysis steps.

Value

GSEA results.

See Also

plot_gsea

Examples

```
# Get example CEMiTool object
data(cem)
# Look at example annotation file
sample_annotation(cem)
# Run GSEA on network modules
cem <- mod_gsea(cem)
# Check results
gsea_data(cem)
```

---

mod_names *Get module names in a CEMiTool object*

Description

Get module names in a CEMiTool object

Usage

```
mod_names(cem, include_NC = TRUE)

## S4 method for signature 'CEMiTool'
mod_names(cem, include_NC = TRUE)
```

Arguments

cem	Object of class CEMiTool
include_NC	Logical. Whether or not to include "Not.Correlated" module. Defaults to TRUE.

Value

Module names

Examples

```
# Get example CEMiTool object
data(cem)
# Get module names
mod_names(cem)
```

`mod_ora` *Module Overrepresentation Analysis*

Description

Performs overrepresentation analysis for each co-expression module found.

Usage

```
mod_ora(cem, ...)

## S4 method for signature 'CEMiTool'
mod_ora(cem, gmt, verbose = FALSE)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`gmt`	Object of class `data.frame` with 2 columns, one with pathways and one with genes
`verbose`	logical. Report analysis steps.

Value

Object of class `CEMiTool`

Examples

```
# Get example CEMiTool object
data(cem)
# Read gmt file
gmt <- read_gmt(system.file('extdata', 'pathways.gmt',
                  package='CEMiTool'))
# Run module overrepresentation analysis
cem <- mod_ora(cem, gmt)
# Check results
head(ora_data(cem))
```

mod_summary *Co-expression module summarization*

Description

Summarizes modules using mean or eigengene expression.

Usage

```
mod_summary(cem, ...)

## S4 method for signature 'CEMiTool'
mod_summary(cem, method = c("mean", "median",
  "eigengene"), verbose = FALSE)
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
method	A character string indicating which summarization method is to be used. Can be 'eigengene', 'mean' or 'median'. Default is 'mean'.
verbose	Logical. If TRUE, reports analysis steps.

Value

A data.frame with summarized values.

Examples

```
# Get example CEMiTool object
data(cem)
# Summarize results
mod_summary <- mod_summary(cem)
```

new_cem *Create a CEMiTool object*

Description

Create a CEMiTool object

Usage

```
new_cem(expr = data.frame(), sample_annot = data.frame(),
  sample_name_column = "SampleName", class_column = "Class")
```

Arguments

expr	Object of class data.frame with gene expression data
sample_annot	Object of data.frame containing the sample annotation. It should have at least two columns containing group Class and the Sample Name that should match with samples in expression file
sample_name_column	A string specifying the column to be used as sample identification. Default: "SampleName".
class_column	A string specifying the column to be used as a grouping factor for samples. Default: "Class"

Value

Object of class CEMiTool

Examples

```
# Create new CEMiTool object
cem <- new_cem()
# Create new CEMiTool object with expression and sample_annotation data
data(expr0)
data(sample_annot)
cem <- new_cem(expr0, sample_annot, "SampleName", "Class")
# Equivalent to a call to new()
cem2 <- new("CEMiTool", expression=expr0, sample_annotation=sample_annot)
identical(cem, cem2)
```

---

nmodules *Get the number of modules in a CEMiTool object*

Description

Get the number of modules in a CEMiTool object

Usage

```
nmodules(cem)

## S4 method for signature 'CEMiTool'
nmodules(cem)
```

Arguments

cem	Object of class CEMiTool

Value

number of modules

Examples

```
# Get example CEMiTool object
data(cem)
# Get the number of modules
nmodules(cem)
```

`ora_data` *Retrieve over representation analysis (ORA) results*

Description

Retrieve over representation analysis (ORA) results

Usage

```
ora_data(cem)

## S4 method for signature 'CEMiTool'
ora_data(cem)
```

Arguments

`cem`	Object of class `CEMiTool`

Value

Object of class `data.frame` with ORA data

Examples

```
# Get example CEMiTool object
data(cem)
# Read gmt file
gmt <- read_gmt(system.file('extdata', 'pathways.gmt',
                  package='CEMiTool'))
# Run module overrepresentation analysis
cem <- mod_ora(cem, gmt)
# Check results
head(ora_data(cem))
```

plot_beta_r2 *Soft-threshold beta selection graph*

Description

Creates a graph showing each possible soft-threshold value and its corresponding R squared value

Usage

```
plot_beta_r2(cem, ...)

## S4 method for signature 'CEMiTool'
plot_beta_r2(cem,
  title = "Scale independence (beta selection)")
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
title	title of the graph

Value

Object of class CEMiTool with beta x R squared plot

Examples

```
# Get example CEMiTool object
data(cem)
# Plot scale-free model fit as a function of the soft-thresholding beta parameter choice
cem <- plot_beta_r2(cem)
# Check resulting plot
show_plot(cem, "beta_r2")
```

plot_gsea *GSEA visualization*

Description

Creates a heatmap with the results of gene set enrichment analysis (GSEA) of co-expression modules

Usage

```
plot_gsea(cem, ...)

## S4 method for signature 'CEMiTool'
plot_gsea(cem, pv_cut = 0.05)
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
pv_cut	P-value cut-off. Default 0.05

Value

Object of class CEMiTool with GSEA plots

Examples

```
# Get example CEMiTool object
data(cem)
# Get example sample annotation file
# Run GSEA on network modules
cem <- mod_gsea(cem)
# Plot GSEA results
cem <- plot_gsea(cem)
# Check resulting plot
show_plot(cem, "gsea")
```

---

plot_hist *Plot histogram*

Description

This function plots a histogram of the distribution of gene expression, to help assess the normality of the data.

Usage

```
plot_hist(cem, ...)

## S4 method for signature 'CEMiTool'
plot_hist(cem, filtered = FALSE)
```

Arguments

cem	Object of class CEMiTool
...	Optional parameters
filtered	Logical. Whether or not to use filtered data for CEMiTool objects (Default: FALSE).

Value

Object of class CEMiTool containing expression histogram

Examples

```
# Get example CEMiTool object
data(cem)
# Plot histogram
cem <- plot_hist(cem)
# Check results
show_plot(cem, "hist")
```

`plot_interactions` *Network visualization*

Description

Creates a graph based on interactions provided

Usage

```
plot_interactions(cem, ...)

## S4 method for signature 'CEMiTool'
plot_interactions(cem, n = 10, ...)
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`n`	number of nodes to label

Value

Object of class `CEMiTool` with profile plots

Examples

```
# Get example CEMiTool object
data(cem)
# Get example gene interactions data
int <- system.file("extdata", "interactions.tsv", package = "CEMiTool")
int_df <- read.delim(int)
# Include interaction data into CEMiTool object
interactions_data(cem) <- int_df
# Plot resulting networks
cem <- plot_interactions(cem)
# Check resulting plot
show_plot(cem, "interaction")
```

plot_mean_k *Network mean connectivity*

Description

Creates a graph showing the mean connectivity of genes in the network

Usage

```
plot_mean_k(cem, ...)

## S4 method for signature 'CEMiTool'
plot_mean_k(cem, title = "Mean connectivity")
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters.
title	title of the graph

Value

Object of class CEMiTool with connectivity plot

Examples

```
# Get example CEMiTool object
data(cem)
# Plot scale-free model fit as a function of the soft-thresholding beta parameter choice
cem <- plot_mean_k(cem)
# Check resulting plot
show_plot(cem, "mean_k")
```

plot_mean_var *Plot mean and variance*

Description

This plot returns a scatterplot of the mean by the variance of gene expression. A linear relationship between these values for RNAseq data suggest that an appropriate transformation such as the Variance Stabilizing Transformation should be applied.

Usage

```
plot_mean_var(cem, ...)

## S4 method for signature 'CEMiTool'
plot_mean_var(cem, filtered = FALSE)
```

Arguments

cem	Object of class CEMiTool
...	Optional parameters
filtered	Logical. Whether or not to use filtered data for CEMiTool objects (Default: FALSE).

Value

Object of class CEMiTool containing a mean and variance plot

Examples

```
# Get example CEMiTool object
data(cem)
# Plot mean and variance plot
cem <- plot_mean_var(cem)
# Check results
show_plot(cem, 'mean_var')
```

---

plot_ora *ORA visualization*

Description

Creates a bar plot with the results of module overrepresentation analysis

Usage

```
plot_ora(cem, ...)

## S4 method for signature 'CEMiTool'
plot_ora(cem, n = 10, pv_cut = 0.05, ...)
```

Arguments

cem	Object of class CEMiTool.
...	parameters to plot_ora_single
n	number of modules to show
pv_cut	p-value significance cutoff. Default is 0.05.

Value

Object of class CEMiTool with ORA plots

Examples

```
# Get example CEMiTool object
data(cem)
# Read example gmt file
gmt <- read_gmt(system.file('extdata', 'pathways.gmt',
                  package='CEMiTool'))
# Run overrepresentation analysis
cem <- mod_ora(cem, gmt)
# Plot module gene expression profiles
cem <- plot_ora(cem)
# Check resulting plot
show_plot(cem, "ora")
```

`plot_profile` *Expression profile visualization*

Description

Creates a plot with module gene expression profiles along samples

Usage

```
plot_profile(cem, ...)

## S4 method for signature 'CEMiTool'
plot_profile(cem, order_by_class = TRUE,
  center_func = "mean")
```

Arguments

`cem`	Object of class `CEMiTool`.
`...`	Optional parameters.
`order_by_class`	Logical. Only used if a sample annotation file is present. Whether or not to order by the class column in the sample annotation file (as defined by the class_column slot in `cem`).
`center_func`	Character string indicating the centrality measure to show in the plot. Either 'mean' (the default) or 'median'.

Value

Object of class `CEMiTool` with profile plots

Examples

```
# Get example CEMiTool object
data(cem)
# Plot module gene expression profiles
cem <- plot_profile(cem)
# Check resulting plot
show_plot(cem, "profile")
```

plot_qq *Plot quantile-quantile plot*

Description

This function creates a normal QQ plot of the expression values.

Usage

```
plot_qq(cem, ...)

## S4 method for signature 'CEMiTool'
plot_qq(cem, filtered = FALSE)
```

Arguments

cem	Object of class CEMiTool
...	Optional parameters
filtered	Logical. Whether or not to use filtered data for CEMiTool objects (Default: FALSE).

Value

Object of class CEMiTool containing qqplot

Examples

```
# Get example CEMiTool object
data(cem)
# Plot quantile-quantile plot
cem <- plot_qq(cem)
# Check results
show_plot(cem, 'qq')
```

plot_sample_tree *Sample clustering*

Description

Creates a dendrogram showing the similarities between samples in the expression data.

Usage

```
plot_sample_tree(cem, ...)

## S4 method for signature 'CEMiTool'
plot_sample_tree(cem, col_vector = NULL,
  sample_name_column = NULL, class_column = NULL, filtered = FALSE)
```

Arguments

cem	Object of class CEMiTool or data.frame.
...	Optional parameters.
col_vector	A vector of columns to use for visualizing the clustering. See Details.
sample_name_column	A string specifying the column to be used as sample identification. For CEMiTool objects, this will be the string specified in the sample_name_column slot.
class_column	A string specifying the column to be used as sample group identification. For CEMiTool objects, this will be the string specified in the class_column slot.
filtered	Logical. Whether or not to use filtered data for CEMiTool objects (Default: FALSE).

Value

Object of class CEMiTool with dendrogram or a plot object.

Examples

```
# Get example CEMiTool object
data(cem)
# Plot sample dendrogram
cem <- plot_sample_tree(cem)
# Check resulting plot
show_plot(cem, "sample_tree")
```

---

read_gmt *Read a GMT file*

Description

Read a GMT file

Usage

```
read_gmt(fname)
```

Arguments

fname	GMT file name.

Value

A list containing genes and description of each pathway

Examples

```
# Read example gmt file
gmt_fname <- system.file("extdata", "pathways.gmt", package = "CEMiTool")
gmt_in <- read_gmt(gmt_fname)
```

sample_annot *Yellow Fever Sample Annotation data*

Description

Modified data from a yellow fever vaccination study by Querec et al, 2009. This dataset, together with `expr` can be used as input for CEMiTool functions

Usage

```
data(sample_annot)
```

Format

An object of class `data.frame`

Source

GEO

References

Querec TD, Akondy RS, Lee EK, Cao W et al. Systems biology approach predicts immunogenicity of the yellow fever vaccine in humans. Nat Immunol 2009 Jan;10(1):116-25. PMID: 19029902 PubMed

Examples

```
data(expr)
data(sample_annot)
# Run CEMiTool analysis
## Not run: cemitool(expr, sample_annot)
```

sample_annotation *Retrive or set the sample_annotation attribute*

Description

Retrive or set the sample_annotation attribute

Usage

```
sample_annotation(cem)

## S4 method for signature 'CEMiTool'
sample_annotation(cem)

sample_annotation(cem, sample_name_column = "SampleName",
  class_column = "Class") <- value

## S4 replacement method for signature 'CEMiTool'
sample_annotation(cem, sample_name_column = "SampleName",
  class_column = "Class") <- value
```

Arguments

cem	Object of class CEMiTool
sample_name_column	A string containing the name of a column which should be used as a unique identifier for samples in the file. Only used when assigning a sample annotation data.frame. Default: "SampleName".
class_column	A string containing the name of a column which should be used to identify different sample groups. Only used when assigning a sample annotation data.frame. Default: "Class"
value	A data.frame containing the sample annotation, should have at least two columns containing the Class and the Sample Name that should match with samples in expression

Value

A data.frame containing characteristics of each sample.

Examples

```
# Get example expression data
data(expr0)
# Get example sample_annotation data
data(sample_annot)
# Initialize CEMiTool object with expression
cem <- new_cem(expr0)
# Add sample annotation file to CEMiTool object
sample_annotation(cem,
    sample_name_column="SampleName",
    class_column="Class") <- sample_annot
# Check annotation
head(sample_annotation(cem))
```

---

save_plots *Save CEMiTool object plots*

Description

Save plots into the directory specified by the directory argument.

Usage

```
save_plots(cem, ...)

## S4 method for signature 'CEMiTool'
save_plots(cem, value = c("all", "profile", "gsea",
  "ora", "interaction", "beta_r2", "mean_k", "sample_tree", "mean_var", "hist",
  "qq"), force = FALSE, directory = "./Plots")
```

Arguments

cem	Object of class CEMiTool.
...	Optional parameters One of "all", "profile", "gsea", "ora", "interaction", "beta_r2", "mean_k", "sample_tree", "mean_var", "hist", "qq".
value	A character string containing the name of the plot to be saved.
force	If the directory exists, execution will not stop.
directory	Directory into which the files will be saved.

Value

A pdf file or files with the desired plot(s)

Examples

```
# Get example CEMiTool object
data(cem)
# Plot beta x R squared graph
cem <- plot_beta_r2(cem)
# Save plot
## Not run: save_plots(cem, value="beta_r2", directory="./Plots")
```

---

show,CEMiTool-method *Print a cemitool object*

Description

Print a cemitool object

Usage

```
## S4 method for signature 'CEMiTool'
show(object)
```

Arguments

object	Object of class CEMiTool

Value

A CEMiTool object.

show_plot *Retrieve CEMiTool object plots*

Description

Retrieve CEMiTool object plots

Usage

```
show_plot(cem, value)

## S4 method for signature 'CEMiTool'
show_plot(cem, value = c("profile", "gsea", "ora",
  "interaction", "beta_r2", "mean_k", "sample_tree", "mean_var", "hist", "qq"))
```

Arguments

cem	Object of class CEMiTool.
value	A character string containing the name of the plot to be shown. One of "profile", "gsea", "ora", "interaction", "beta_r2", "mean_k", "sample_tree", "mean_var", "hist", "qq".

Value

A plot corresponding to a CEMiTool analysis

Examples

```
# Get example CEMiTool object
data(cem)
# Plot beta x R squared graph
cem <- plot_beta_r2(cem)
# Check plot
show_plot(cem, "beta_r2")
```

StatQqLine *ggplot2-ggproto*

Description

ggplot2-ggproto

`write_files` *Save the CEMiTool object in files*

Description

Save the CEMiTool object in files

Usage

```
write_files(cem, ...)

## S4 method for signature 'CEMiTool'
write_files(cem, directory = "./Tables", force = FALSE)
```

Arguments

`cem`	Object of class `CEMiTool`
`...`	Optional parameters
`directory`	a directory
`force`	if the directory exists the execution will not stop

Value

A directory containing CEMiTool results in files.

Examples

```
## Not run:
# Get example CEMiTool object
data(cem)
# Save CEMiTool results in files
write_files(cem, directory=".", force=TRUE)

## End(Not run)
```

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