

Package ‘meaca’

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Type Package

Title Mixed-effects Enrichment Analysis with Correlation Adjusted

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Description This package produces all results needed in the paper
Use four spaces when indenting paragraphs within the Description.

Depends R (>= 3.2.1)

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imports dplyr,
ggplot2

LazyData true

Encoding UTF-8

RoxygenNote 5.0.1

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btw_gene_corr	<i>Estimate sample correlation.</i>
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Description

Average correlations for genes

Usage

```
btw_gene_corr(expression_data, trt, geneset, standardize = T,
  minSetSize = 5)
```

Arguments

expression_data	the expressoin matrix.
trt	treatment labels
geneset	an object from read_gene_set
standardize	'TRUE' or 'FALSE', whether the data should be standarized
minSetSize	the minimum number of genes contained for a gene set to be considered.

Value

a list	
set_name	The name of the gene set
testSetCor	Average correlation for genes in the test set
interCor	Average correlation between genes in the test set and those not in the test set
backSetCor	Average correlations for genes not in the test set.

data_simu	<i>Compare meaca to existing methods</i>
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Description

Produce p value matrix for simulation discussed in the paper.

Usage

```
data_simu(nsim = 1000, ncore = 6, package_used = c("MASS", "qusage"),
  verbose_show = FALSE, meaca_only = FALSE, file_to_source = NULL,
  dest = getwd(), n_gene = 500, n_test = 100, prop = c(0.1, 0.1),
  rho1 = 0.1, rho2 = 0.05, rho3 = -0.05, size = 50, de_mu = 2,
  de_sd = 1, data_gen_method = "chol", seed = 123)
```

Arguments

nsim	number of simulation to run
ncore	number of CPUs to be used in the parallel simulation
package_used	the packages to be used in the simulation
verbose_show	for debug purpose, set to 'FALSE' if not in debug mode
meaca_only	Should all the methods to be compared? If 'TRUE', produce Figure 1; otherwise Figure 2
file_to_source	the R files containing functions to be sourced
dest	where to store the results
n_gene	total number of genes to be simulated
n_test	number of genes in the test set.
prop	a vector of length 2, proportion of DE genes within go term and outside go_term, corresponding to \$p_t\$ and \$p_b\$.
rho1	a scalar, correlation between two test genes (i.e., ρ_1 in the paper)
rho2	a scalar, correlation between two background genes (i.e., ρ_2 in the paper)
rho3	correlation between a test gene and a background gene (i.e., ρ_3 in the paper)
size	number of samples to be simulated
de_mu, de_sd	if the gene is DE, $\delta \sim N(\text{de_mu}, \text{de_sd})$
data_gen_method	data generation method; if 'data_gen_method = MASS', then mvnrm is used, otherwise see function rmvnorm
seed	the seed used for simulation (for reproducibility purpose)
seed	the seed used for simulation (for reproducibility purpose)

Value

a text file containing the p value matrix

estimate_sigma	<i>Estimate sample covariance.</i>
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Description

Estimate sample covariance and calculate the gene-level statistics

Usage

```
estimate_sigma(expression_data, trt)
```

Arguments

expression_data	the expression matrix.
trt	sample labels. 0 for control and 1 for treatment

Value

a list

sigma a covariance matrix

t_val a vector of gene level test statistics

meaca_multiple *meaca-multiple.*

Description

meaca for testing multiple gene sets.

Usage

```
meaca_multiple(expression_data, trt, geneset, standardize = T,
  minSetSize = 5, fdr_method = "BH")
```

Arguments

expression_data the expressoin matrix.

trt treatment labels.

geneset gene sets to be tested, an object from read_gene_set.

standardize whether the data should be standaridzed.

minSetSize the minimum number of genes contained for a gene set to be considered.

fdr_method which method is ued to adjust the p values. see arguments in function p.adjust.

Value

a data frame

meaca_single *meaca-single.*

Description

meaca for single gene set test.

Usage

```
meaca_single(expression_data, trt, go_term, standardize = F)
```

Arguments

expression_data the expressoin matrix.

trt treatment labels.

go_term an indicator vector. 1 for genes in the test, 0 otherwise.

standardize whether the data should be standaridzed.

Value

a list	
stat	the test statistic
p1	chi-square test p value
status	"up" or "down", the direction of differential expression
p2	two-sided test p-value using normal distribution

Examples

```
t1 <- simulate_expression_data(size = 50, n_gene = 500, n_test = 100,
                              prop = c(0.1, 0.1), de_mu = 2, de_sd = 1,
                              rho1 = 0.1, rho2 = 0.05, rho3 = -0.05,
                              data_gen_method = "chol", seed = 123)
meaca_single(t1$data, trt = t1$trt, go_term = t1$go_term)
```

read_gene_set	<i>Convert gene sets to lists</i>
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Description

read the gene sets of the MsigDB format.

Usage

```
read_gene_set(msigdb)
```

Arguments

msigdb	gene set ensemble downloaded from broad institute see https://www.gsea-msigdb.org/gsea/doc/GSEAUserGuideFrame.html .
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Value

a list	
total	number of gene sets contained.
size	a numerical vector containing the size of each gene set.
gene_set	a list. The first element is the set name. From the third element each containing members of the gene set.

```
simulate_expression_data
```

Simulate expression data.

Description

simulate normally distributed expression data with desired DE probabilities for genes in the test set and for those not in the test set..

Usage

```
simulate_expression_data(size, n_gene, n_test, prop, de_mu, de_sd, rho1, rho2,
  rho3, data_gen_method = "chol", seed = 123)
```

Arguments

size	number of samples to be simulated
n_gene	total number of genes to be simulated
n_test	number of genes in the test set.
prop	a vector of length 2, proportion of DE genes within go term and outside go_term, corresponding to \$p_t\$ and \$p_b\$.
de_mu, de_sd	if the gene is DE, $\delta \sim N(\text{de_mu}, \text{de_sd})$
rho1	a scalar, correlation between two test genes (i.e., ρ_1 in the paper)
rho2	a scalar, correlation between two background genes (i.e., ρ_2 in the paper)
rho3	correlation between a test gene and a background gene (i.e., ρ_3 in the paper)
data_gen_method	data generation method; if 'data_gen_method = MASS', then mvnrm is used, otherwise see function rmvnorm
seed	the seed used for simulation (for reproducibility purpose)

Value

a list	
data	a expression matrix of $m \times n$ where m is the number of genes and n is the number of samples.
trt	sample labels of length n, 1 for treatment and 0 for control.
go_term	gene labels of length m, 1 for go_term genes and 0 otherwise.
sigma	true covariance matrix upon which data is simulated.

Examples

```
t1 <- simulate_expression_data(size = 50, n_gene = 500, n_test = 100,
  prop = c(0.1, 0.1), de_mu = 2, de_sd = 1,
  rho1 = 0.1, rho2 = 0.05, rho3 = -0.05,
  data_gen_method = "chol", seed = 123)
```

`standardize_expression_data`*standardize expression data, with method described in the paper.*

Description

Standardize the expression data.

Usage

```
standardize_expression_data(expression_data, trt)
```

Arguments

`expression_data`

the expression matrix.

`trt`

sample labels. 0 for control and 1 for treatment

Value

a matrix of the same dimension as input data.

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