

Package ‘scQTLtools’

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Type Package

Title An R package for single-cell eQTL analysis and visualization

Version 0.99.12

Description This package specializes in analyzing and visualizing eQTL at the single-cell level. It can read gene expression matrices or Seurat data, or SingleCellExperiment object along with genotype data. It offers a function for cis-eQTL analysis to detect eQTL within a given range, and another function to fit models with three methods. Using this package, users can also generate single-cell level visualization result.

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| | |
|--------------------|---|
| scQTLtools-package | <i>scQTLtools: An R package for single-cell eQTL analysis and visualization</i> |
|--------------------|---|

Description

This package specializes in analyzing and visualizing eQTL at the single-cell level. It can read gene expression matrices or Seurat data, or SingleCellExperiment object along with genotype data. It offers a function for cis-eQTL analysis to detect eQTL within a given range, and another function to fit models with three methods. Using this package, users can also generate single-cell level visualization result.

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See Also

Useful links:

- <https://github.com/XFWuCN/scQTLtools>
- Report bugs at <https://github.com/XFWuCN/scQTLtools/issues>

| | |
|----------------|--|
| adjust_pvalues | <i>Adjust p-values and perform threshold filtering based on the adjusted p-values.</i> |
|----------------|--|

Description

Adjust p-values and perform threshold filtering based on the adjusted p-values.

Usage

```
adjust_pvalues(result, pAdjustMethod = "bonferroni", pAdjustThreshold = 0.05)
```

Arguments

| | |
|------------------|---|
| result | Dataframe that contains gene-SNP pairs' information. |
| pAdjustMethod | Methods for p-value adjusting, one of "bonferroni", "holm", "hochberg", "holmel" or "BH". The default option is "bonferroni". |
| pAdjustThreshold | Only SNP-Gene pairs with adjusted p-values meeting the threshold will be displayed. Default by 0.05. |

Value

A dataframe that has been adjusted and filtered, containing information on gene-SNP pairs.

Examples

```
example_data <- data.frame(  
  gene = c("Gene1", "Gene2", "Gene3", "Gene4"),  
  SNP = c("SNP1", "SNP2", "SNP3", "SNP4"),  
  pvalue = c(0.001, 0.04, 0.03, 0.0005))  
pAdjustMethod <- "BH"  
pAdjustThreshold <- 0.05  
adjusted_result <- adjust_pvalues(example_data, pAdjustMethod,  
  pAdjustThreshold)
```

| | |
|-----------|--------------------------|
| buildZINB | <i>Build zinb model.</i> |
|-----------|--------------------------|

Description

Build zinb model.

Usage

```
buildZINB(counts)
```

Arguments

counts a vector for gene expression.

Value

Four parameters

Examples

```
data(testGene)  
gene <- unlist(testGene[1, ])  
result <- buildZINB(gene)
```

| | |
|---------|--|
| callQTL | <i>callQTL: Uncover single-cell eQTLs exclusively using scRNA-seq data. A function designed to identify eQTLs from scRNA-seq data.</i> |
|---------|--|

Description

callQTL: Uncover single-cell eQTLs exclusively using scRNA-seq data. A function designed to identify eQTLs from scRNA-seq data.

Usage

```
callQTL(
  eQTLObject,
  gene_ids = NULL,
  downstream = NULL,
  upstream = NULL,
  gene_mart = NULL,
  snp_mart = NULL,
  pAdjustMethod = "bonferroni",
  useModel = "zinb",
  pAdjustThreshold = 0.05,
  logfcThreshold = 0.1
)
```

Arguments

| | |
|------------------|---|
| eQTLObject | An S4 object of class eQTLObject. |
| gene_ids | A gene ID or a list of gene IDS. |
| downstream | Being used to match SNPs within a base range defined by the start position of genes. |
| upstream | Being used to match SNPs within a base range defined by the end position of genes. |
| gene_mart | An object of class Mart representing the BioMart database to connect to. If NULL, the function will use the Ensembl Gene BioMart. |
| snp_mart | An object of class Mart representing the BioMart database to connect to. If NULL, the function will use the Ensembl SNP BioMart. |
| pAdjustMethod | Methods for p-value adjusting, one of 'bonferroni', 'holm', 'hochberg', 'hommel' or 'BH'. Default by 'bonferroni'. |
| useModel | Model for fitting dataframe, one of 'poission', 'zinb', or 'linear'. |
| pAdjustThreshold | Only SNP-Gene pairs with adjusted p-values meeting the threshold will be displayed. Default by 0.05. |
| logfcThreshold | Represents the minimum beta threshold for fitting SNP-Gene pairs. |

Value

A dataframe, each row describes eQTL discovering result of a SNP-Gene pair.

Examples

```
data(testEQTL)
library(biomaRt)
gene_mart <- useEnsembl(biomart = "genes",
                       dataset = "hsapiens_gene_ensembl",
                       mirror = 'asia')
snp_mart <- useEnsembl(biomart = "snps",
```

```

                                dataset = "hsapiens_snp",
                                mirror = 'asia')
eqtl <- callQTL(
  eQTLObject = testEQTL,
  gene_ids = NULL,
  downstream = NULL,
  upstream = NULL,
  gene_mart = gene_mart,
  snp_mart = snp_mart,
  pAdjustMethod = 'bonferroni',
  useModel = 'linear',
  pAdjustThreshold = 0.05,
  logfcThreshold = 0.025
)

```

| | |
|--------------|---|
| checkSNPList | <i>Check if the SNP ids in the input genotype matrix are valid.</i> |
|--------------|---|

Description

Check if the SNP ids in the input genotype matrix are valid.

Usage

```
checkSNPList(snpList, snp_mart = NULL, snpDataset = "hsapiens_snp")
```

Arguments

| | |
|------------|--|
| snpList | a list of SNPs id. |
| snp_mart | An object of class ‘Mart’ representing the BioMart database connect to for SNPs. If provided, this should be a ‘Mart’ object obtained by calling ‘useEnsembl()’, which allows specifying a mirror in case of connection issues. If ‘NULL’, the function will create and use a ‘Mart’ object pointing to the Ensembl SNP BioMart using the specified ‘snpDataset’ and a default mirror. |
| snpDataset | A character string specifying the SNP dataset to use from ENSEMBL. The default is ‘hsapiens_snp’ for human SNPs. |

Value

SNP location dataframe

Examples

```

data(testSNP2)
snpList <- rownames(testSNP2)
snpDataset <- 'hsapiens_snp'
snps_loc <- checkSNPList(snpList = snpList,
                        snpDataset = snpDataset)

```

CPM_normalize *Normalize the gene expression matrix with CPM.*

Description

'CPM_normalize()' scales an expression matrix using Counts Per Million (CPM) normalization, applying logarithm and scaling operations to adjust data.

Usage

```
CPM_normalize(expressionMatrix)
```

Arguments

expressionMatrix
 Input raw gene expression matrix.

Value

A gene expression matrix after normalized.

Examples

```
data(testGene)  
CPM_normalize(testGene)
```

createGeneLoc *Create gene location dataframe.*

Description

Create gene location dataframe.

Usage

```
createGeneLoc(  
  geneList,  
  gene_mart = NULL,  
  geneDataset = "hsapiens_gene_ensembl",  
  OrgDb  
)
```


Arguments

| | |
|-------------|--|
| geneList | A gene id or a list of genes id. |
| gene_mart | An object of class 'Mart' representing the BioMart database connect to for gene. If provided, this should be a 'Mart' object obtained by calling 'useEnsembl()', which allows specifying a mirror in case of connection issues. If 'NULL', the function will create and use a 'Mart' object pointing to the Ensembl Gene BioMart using the specified 'geneDataset' and a default mirror. |
| geneDataset | A character string specifying the gene dataset to use from ENSEMBL. The default is "hsapiens_gene_ensembl" for human genes. |
| OrgDb | OrgDb name:"org.Hs.eg.db", "org.Mm.eg.db". |

Value

data.frame

Examples

```
data(testGene)
geneList <- rownames(testGene)
library(GOsemSim)
library(biomaRt)
OrgDb <- load_OrgDb("org.Hs.eg.db")
gene_mart <- useEnsembl(biomart = "genes",
                       dataset = "hsapiens_gene_ensembl",
                       mirror = 'asia')
gene_loc <- createGeneLoc(geneList = geneList,
                         gene_mart = gene_mart,
                         OrgDb = OrgDb)
```

| | |
|-----------------|---|
| createQTLObject | <i>createObject: Create the eQTLObject. We next create a S4 object. The object serves as a container that contains both data (like the count matrix) and meta.data.</i> |
|-----------------|---|

Description

createObject: Create the eQTLObject. We next create a S4 object. The object serves as a container that contains both data (like the count matrix) and meta.data.

Usage

```
createQTLObject(
  snpMatrix,
  genedata,
  biClassify = FALSE,
  species = NULL,
  group = NULL,
  ...
)
```

Arguments

| | |
|------------|--|
| snpMatrix | A genotype matrix where each row is one variant and each column is one sample, and the scoring method is 0/1/2/3. |
| genedata | A gene expression matrix or a Seurat object, or a SingleCellExperiment object. |
| biClassify | The user chooses whether to convert the counting method of the snpMatrix to 0/1/2, TRUE indicates conversion, and FALSE indicates no conversion, default is no conversion. |
| species | The species that the user wants to select, human or mouse. |
| group | Provided by Seurat's meta.data, such as celltypes, cellstatus and so on. By default, it is NULL. |
| ... | other parameters |

Value

eQTLObject

Examples

```
data(testSNP)
data(testGene)
eqtl <- createQTLObject(snpMatrix = testSNP,
                        genedata = testGene,
                        biClassify = FALSE,
                        species = 'human',
                        group = NULL)
```

createSNPsLoc

Create SNP location dataframe.

Description

Create SNP location dataframe.

Usage

```
createSNPsLoc(snpList, snp_mart = NULL, snpDataset = "hsapiens_snp")
```

Arguments

| | |
|------------|--|
| snpList | a list of SNPs id. |
| snp_mart | An object of class 'Mart' representing the BioMart database connect to for SNPs. If provided, this should be a 'Mart' object obtained by calling 'useEnsembl()', which allows specifying a mirror in case of connection issues. If 'NULL', the function will create and use a 'Mart' object pointing to the Ensembl SNP BioMart using the specified 'snpDataset' and a default mirror. |
| snpDataset | A character string specifying the SNP dataset to use from ENSEMBL. The default is 'hsapiens_snp' for human SNPs. |

Value

data.frame

Examples

```
snpList <- c('rs546', 'rs549', 'rs568', 'rs665', 'rs672')
library(biomaRt)
snp_mart <- useEnsembl(biomart = "snps",
                      dataset = "hsapiens_snp",
                      mirror = 'asia')
snp_loc <- createSNPsLoc(snpList = snpList,
                        snp_mart = snp_mart)
```

| | |
|-----------------|---|
| DESeq_normalize | <i>Normalize the gene expression matrix with DESeq.</i> |
|-----------------|---|

Description

'DESeq_normalize()' normalizes an expression matrix using the DESeq2 package.

Usage

```
DESeq_normalize(expressionMatrix)
```

Arguments

expressionMatrix
Input raw gene expression matrix.

Value

A gene expression matrix after normalized.

Examples

```
data(testGene)
DESeq_normalize(testGene)
```

| | |
|--------------|--|
| draw_boxplot | <i>Generate a boxplot of expression levels by SNP factor</i> |
|--------------|--|

Description

'draw_boxplot()' creates a boxplot visualizing expression levels across different SNP factors in the dataframe. It uses ggplot2 to produce a plot with customizable aesthetics for clarity and presentation.

Usage

```
draw_boxplot(df, unique_group)
```

Arguments

| | |
|--------------|---|
| df | Data frames listed as gene expression data, genotype data, and groups |
| unique_group | name of unique group |

Value

ggplot

Examples

```
set.seed(123)
counts_Ref <- rnorm(50, mean = 10, sd = 2)
counts_Alt <- rnorm(50, mean = 12, sd = 2)
i <- rep("GroupA", 100)
unique_group <- unique(i)
dataframe <- data.frame(
  expression = c(counts_Ref, counts_Alt),
  snp = c(rep("REF", length(counts_Ref)),
          rep("ALT", length(counts_Alt))), group = i)
dataframe$snp <- factor(dataframe$snp, levels = c("REF", "ALT"))
draw_boxplot(df = dataframe, unique_group = unique_group)
```

| | |
|---------------|---|
| draw_histplot | <i>Generate a hist plot of expression levels by SNP factor.</i> |
|---------------|---|

Description

'draw_histplot()' generates histograms using ggplot2, displaying the distribution of expression values categorized by SNP type.

Usage

```
draw_histplot(df, unique_group)
```

Arguments

df Data frames listed as gene expression data, genotype data, and groups
 unique_group name of unique group

Value

ggplot

Examples

```
set.seed(123)
counts_Ref <- rnorm(50, mean = 10, sd = 2)
counts_Alt <- rnorm(50, mean = 12, sd = 2)
i <- rep("GroupA", 100); unique_group <- unique(i)
dataframe <- data.frame(expression = c(counts_Ref, counts_Alt),
                        snp = c(rep("REF", length(counts_Ref)),
                               rep("ALT", length(counts_Alt))), group = i)
dataframe$snp <- factor(dataframe$snp, levels = c("REF", "ALT"))
draw_histplot(df = dataframe, unique_group = unique_group)
```

draw_QTLplot *Create a combined plot with violin, boxplot, and scatter point overlay.*

Description

‘draw_QTLplot()’ generates a combined plot using ggplot2, showing the distribution of expression values across different SNPs. It combines a violin plot, boxplot, and scatter points for each SNP category.

Usage

```
draw_QTLplot(df, unique_group)
```

Arguments

df Data frames listed as gene expression data, genotype data, and groups
 unique_group name of unique group

Value

ggplot

Examples

```
set.seed(123)
counts_Ref <- rnorm(50, mean = 10, sd = 2)
counts_Alt <- rnorm(50, mean = 12, sd = 2)
i <- rep("GroupA", 100);unique_group <- unique(i)
dataframe <- data.frame(expression = c(counts_Ref, counts_Alt),
                        snp = c(rep("REF", length(counts_Ref)),
                               rep("ALT", length(counts_Alt))), group = i)
dataframe$snp <- factor(dataframe$snp, levels = c("REF", "ALT"))
draw_QTLplot(df = dataframe, unique_group = unique_group)
```

draw_violinplot

Generate a violin plot of expression levels by SNP factor

Description

‘draw_violinplot()’ creates a violin plot visualizing expression levels across different SNP factors in the dataframe. It uses ggplot2 to produce a plot with customizable aesthetics for clarity and presentation.

Usage

```
draw_violinplot(df, unique_group)
```

Arguments

| | |
|--------------|---|
| df | Data frames listed as gene expression data, genotype data, and groups |
| unique_group | name of unique group |

Value

ggplot

Examples

```
set.seed(123)
counts_Ref <- rnorm(50, mean = 10, sd = 2)
counts_Alt <- rnorm(50, mean = 12, sd = 2)
i <- rep("GroupA", 100);unique_group <- unique(i)
dataframe <- data.frame(expression = c(counts_Ref, counts_Alt),
                        snp = c(rep("REF", length(counts_Ref)),
                               rep("ALT", length(counts_Alt))), group = i)
dataframe$snp <- factor(dataframe$snp, levels = c("REF", "ALT"))
draw_violinplot(df = dataframe, unique_group = unique_group)
```

| | |
|------------------|---|
| eQTLOBJECT-class | <i>Class 'eQTLOBJECT' The eQTLOBJECT class is an R object designed to store data related to eQTL analysis, encompassing data lists, result data frames, and layers for biClassify, species, and grouping information.</i> |
|------------------|---|

Description

Class 'eQTLOBJECT' The eQTLOBJECT class is an R object designed to store data related to eQTL analysis, encompassing data lists, result data frames, and layers for biClassify, species, and grouping information.

Value

eQTLOBJECT

Slots

rawData A gene expression dataframe, the row names represent gene IDs and the column names represent cell IDs.

filterData Gene expression matrix after normalizing.

eQTLResult The result dataframe obtained the sc-eQTL results.

biClassify The user chooses whether to convert the counting method of the snpMatrix to 0, 1, 2, TRUE indicates conversion, and FALSE indicates no conversion, default is no conversion.

species The species that the user wants to select, human or mouse.

groupBy Options for cell grouping, users can choose celltype, cellstatus, etc., depending on meta-data.

useModel model for fitting dataframe.

| | |
|---------------|--|
| filterGeneSNP | <i>filterGeneSNP: Filter gene expression matrix and genotype matrix.</i> |
|---------------|--|

Description

filterGeneSNP: Filter gene expression matrix and genotype matrix.

Usage

```
filterGeneSNP(
  eQTLOBJECT,
  snpNumOfCellsPercent = 10,
  expressionMin = 0,
  expressionNumOfCellsPercent = 10
)
```

Arguments

eQTLObject An S4 object of class eQTLObject.
snpNumOfCellsPercent Only SNPs where cells with each of the different genotypes (REF and ALT, or AA, Aa, and aa) individually account for at least 'snpNumOfCellsPercent' Default by 10.
expressionMin threshold for valid gene expression levels, utilized alongside another parameter, expression.number.of.cells. Default by 0.
expressionNumOfCellsPercent Only genes with expression levels exceeding 'expressionMin' in at least 'expressionNumOfCellsPercent' of cells are considered. The default value is 10.

Value

filtered matrices.

Examples

```

data(testSNP)
data(testGene)
eqtl <- createQTLObject(snpMatrix = testSNP, genedata = testGene)
eqtl <- normalizeGene(eqtl)
eqtl <- filterGeneSNP(eqtl,
  snpNumOfCellsPercent = 2,
  expressionMin = 0,
  expressionNumOfCellsPercent = 2)

```

| | |
|-----------------|--|
| filter_by_abs_b | <i>Filters data frame by absolute b-values, returning rows meeting or exceeding a threshold.</i> |
|-----------------|--|

Description

Filters data frame by absolute b-values, returning rows meeting or exceeding a threshold.

Usage

```
filter_by_abs_b(result, logfcThreshold)
```

Arguments

result Dataframe that contains gene-SNP pairs' information.
logfcThreshold Represents the minimum beta threshold for fitting SNP-Gene pairs. Default by 0.1.

Value

A dataframe filtered by absolute b-values.

Examples

```
example_result <- data.frame(  
  gene = c("Gene1", "Gene2", "Gene3", "Gene4"),  
  SNP = c("SNP1", "SNP2", "SNP3", "SNP4"),  
  b = c(-2.5, 1.0, -0.5, 3.0))  
logfcThreshold <- 0.1  
filtered_result <- filter_by_abs_b(example_result, logfcThreshold)
```

| | |
|-----------------|------------------------------------|
| get_cell_groups | <i>Retrieve Cells by SNP Value</i> |
|-----------------|------------------------------------|

Description

This function extracts the names of cells from a SNP matrix that correspond to a specified value for a given SNP.

Usage

```
get_cell_groups(snpMatrix, SNPid, biClassify)
```

Arguments

| | |
|------------|--|
| snpMatrix | A matrix containing SNP data where rows represent SNPs and columns represent cells. |
| SNPid | A character string or numeric index representing the specific SNP of interest in the SNP matrix. |
| biClassify | The user chooses whether to convert the counting method of the snpMatrix to 0/1/2, TRUE indicates conversion, and FALSE indicates no conversion, default is no conversion. |

Value

A list of cell names (column names of the SNP matrix) that correspond to the specified genotype value for the given SNP.

Examples

```
data(testSNP)  
biClassify <- FALSE  
get_cell_groups(testSNP, "1:632445", biClassify)
```

| | |
|------------|---|
| get_counts | <i>Extract Counts from an Expression Matrix</i> |
|------------|---|

Description

This function retrieves expression counts for a specified gene from an expression matrix, based on the provided list of cells.

Usage

```
get_counts(expressionMatrix, Geneid, cells)
```

Arguments

| | |
|------------------|---|
| expressionMatrix | A matrix containing gene expression data where rows represent genes and columns represent cells. |
| Geneid | A character string or numeric index representing the specific gene of interest in the expression matrix. |
| cells | A character vector of cell names (column names of the expression matrix) from which to extract counts for the specified gene. |

Value

A numeric vector of expression counts for the specified gene in the selected cells.

Examples

```
data(testGene)
get_counts(testGene, "CNN2",
           c("CGGCAGTGTAGCCCTG", "GGAGGATCCCGTTCA"))
```

| | |
|-----------------|--|
| get_filter_data | <i>Generic to access eQTLObjct filter data</i> |
|-----------------|--|

Description

Generic to access eQTLObjct filter data

Usage

```
get_filter_data(x)
```

Arguments

| | |
|---|---------------------|
| x | A eQTLObjct object. |
|---|---------------------|

Value

filtered matrices.

Examples

```
data(testEQTL)
get_filter_data(testEQTL)
```

get_filter_data,eQTLObjct-method
Method to access eQTLObjct filter data

Description

Method to access eQTLObjct filter data

Usage

```
## S4 method for signature 'eQTLObjct'
get_filter_data(x)
```

Arguments

x A eQTLObjct object.

Value

filtered matrices.

get_model_info *Generic to access eQTLObjct used model information*

Description

Generic to access eQTLObjct used model information

Usage

```
get_model_info(x)
```

Arguments

x A eQTLObjct object.

Value

used model information of eQTLObject.

Examples

```
data(testEQTL)
get_model_info(testEQTL)
```

get_model_info, eQTLObject-method

Method to access eQTLObject used model information

Description

Method to access eQTLObject used model information

Usage

```
## S4 method for signature 'eQTLObject'
get_model_info(x)
```

Arguments

x A eQTLObject object.

Value

used model information of eQTLObject.

get_raw_data

Generic to access eQTLObject raw data

Description

Generic to access eQTLObject raw data

Usage

```
get_raw_data(x)
```

Arguments

x A eQTLObject object.

Value

raw data matrix.

Examples

```
data(testEQTL)
get_raw_data(testEQTL)
```

get_raw_data,eQTLObject-method
Method to access eQTLObject raw data

Description

Method to access eQTLObject raw data

Usage

```
## S4 method for signature 'eQTLObject'
get_raw_data(x)
```

Arguments

x A eQTLObject object.

Value

raw data matrix.

get_result_info *Generic to access the result of identifying eQTLs from scRNA-seq data*

Description

Generic to access the result of identifying eQTLs from scRNA-seq data

Usage

```
get_result_info(x)
```

Arguments

x A eQTLObject object.

Value

A dataframe.

Examples

```
data(testEQTL)
get_result_info(testEQTL)
```

get_result_info, eQTLObject-method

Method to access the result of identifying eQTLs from scRNA-seq data

Description

Method to access the result of identifying eQTLs from scRNA-seq data

Usage

```
## S4 method for signature 'eQTLObject'
get_result_info(x)
```

Arguments

x A eQTLObject object.

Value

A dataframe.

initialize_progress_bar

Progress Bar for Model Analysis.

Description

This function initializes a progress bar for use in the 'linearModel', 'poissonModel' and 'zinbModel' function. It is designed to provide feedback on the progress of the analysis by displaying the current step and a percentage completion.

Usage

```
initialize_progress_bar(total, k)
```

Arguments

| | |
|-------|--|
| total | The total number of steps or iterations for which the progress bar will be updated. |
| k | A label or identifier for the specific group or iteration for which the progress bar is being initialized. |

Value

A 'progress_bar' object from the 'progress' package, which is used to track and display the progress.

Examples

```
unique_group <- c("CMP", "GMP")
total_snp_count <- 10 # assume each group have 100 SNP.
pb_model <- lapply(unique_group, function(k) {
  pb <- initialize_progress_bar(total = total_snp_count, k)
  for (i in seq_len(total_snp_count)) {
    Sys.sleep(0.1) # assume progress time
    pb$tick() # update pb
  }
})
```

limma_normalize

Normalize the gene expression matrix with limma

Description

'limma_normalize()' normalizes an expression matrix using the quantile normalization method provided by the limma package.

Usage

```
limma_normalize(expressionMatrix)
```

Arguments

expressionMatrix
Input raw gene expression matrix.

Value

A gene expression matrix after normalized.

Examples

```
data(testGene)
limma_normalize(testGene)
```

| | |
|-------------|---|
| linearModel | <i>Linear model fitting the gene expression matrix and genotype matrix.</i> |
|-------------|---|

Description

Linear model fitting the gene expression matrix and genotype matrix.

Usage

```
linearModel(
  eQTLObject,
  geneIDs,
  snpIDs,
  biClassify = FALSE,
  pAdjustMethod = "bonferroni",
  pAdjustThreshold = 0.05,
  logfcThreshold = 0.1
)
```

Arguments

| | |
|------------------|--|
| eQTLObject | An S4 object of class eQTLObject. |
| geneIDs | Matching genes can be used to fit data. |
| snpIDs | Matching SNPs can be used to fit data. |
| biClassify | The user chooses whether to convert the counting method of the snpMatrix to 0/1/2, TRUE indicates conversion, and FALSE indicates no conversion, default is no conversion. |
| pAdjustMethod | Methods for p-value adjusting, one of "bonferroni", "holm", "hochberg", "hommel" or "BH". The default option is "bonferroni". |
| pAdjustThreshold | Only SNP-Gene pairs with adjusted p-values meeting the threshold will be displayed. Default by 0.05. |
| logfcThreshold | Represents the minimum beta threshold for fitting SNP-Gene pairs. Default by 0.1. |

Value

Dataframe that contains gene-SNP pairs' information.

Examples

```
data(testEQTL)
Gene <- rownames(slot(testEQTL, "filterData")$expMat)
SNP <- rownames(slot(testEQTL, "filterData")$snpMat)
linearResult <- linearModel(
  eQTLObject = testEQTL,
```



```
geneIDs = Gene,  
snpIDs = SNP,  
biClassify = FALSE,  
pAdjustMethod = "bonferroni",  
pAdjustThreshold = 0.05,  
logfcThreshold = 0.025)
```

load_biclassify_info *Generic to access eQTLObject biclassify information*

Description

Generic to access eQTLObject biclassify information

Usage

```
load_biclassify_info(x)
```

Arguments

x A eQTLObject object.

Value

biclassify information of eQTLObject.

Examples

```
data(testEQTL)  
load_biclassify_info(testEQTL)
```

load_biclassify_info, eQTLObject-method
Method to access eQTLObject biclassify information

Description

Method to access eQTLObject biclassify information

Usage

```
## S4 method for signature 'eQTLObject'  
load_biclassify_info(x)
```

Arguments

x A eQTLObject object.

Value

biclassify information of eQTLObject.

| | |
|-----------------|---|
| load_group_info | <i>Generic to access eQTLObject cell grouping information</i> |
|-----------------|---|

Description

Generic to access eQTLObject cell grouping information

Usage

```
load_group_info(x)
```

Arguments

x A eQTLObject object.

Value

A dataframe.

Examples

```
data(testEQTL)
load_group_info(testEQTL)
```

| | |
|------------------------------------|--|
| load_group_info, eQTLObject-method | <i>Method to access eQTLObject cell grouping information</i> |
|------------------------------------|--|

Description

Method to access eQTLObject cell grouping information

Usage

```
## S4 method for signature 'eQTLObject'
load_group_info(x)
```

Arguments

x A eQTLObject object.

Value

A dataframe.

| | |
|-------------------|---|
| load_species_info | <i>Generic to access eQTLObject species information</i> |
|-------------------|---|

Description

Generic to access eQTLObject species information

Usage

```
load_species_info(x)
```

Arguments

x A eQTLObject object.

Value

species information of eQTLObject.

Examples

```
data(testEQTL)
load_species_info(testEQTL)
```

| | |
|--------------------------------------|--|
| load_species_info, eQTLObject-method | <i>Method to access eQTLObject species information</i> |
|--------------------------------------|--|

Description

Method to access eQTLObject species information

Usage

```
## S4 method for signature 'eQTLObject'
load_species_info(x)
```

Arguments

x A eQTLObject object.

Value

species information of eQTLObject.

| | |
|---------------|---|
| log_normalize | <i>Normalize the gene expression matrix with logNormalize method.</i> |
|---------------|---|

Description

'log_normalize()' transforms an expression matrix by applying logarithm and scaling operations to normalize data.

Usage

```
log_normalize(expressionMatrix)
```

Arguments

| | |
|------------------|-----------------------------------|
| expressionMatrix | Input raw gene expression matrix. |
|------------------|-----------------------------------|

Value

A gene expression matrix after normalized.

Examples

```
data(testGene)
log_normalize(testGene)
```

| | |
|---------------|---|
| normalizeGene | <i>normalizeGene: Normalize the gene expression data.</i> |
|---------------|---|

Description

Gene expression matrix normalization is necessary to eliminate technical biases and variabilities, ensuring accurate and comparable analysis of gene expression data. Here we provide 'normalizeGene()' to normalize the data.

Usage

```
normalizeGene(eQTLObject, method = "logNormalize")
```

Arguments

| | |
|------------|---|
| eQTLObject | An S4 object of class eQTLObject. |
| method | Method for normalizing for gene expression dataframe, one of "logNormalize", "CPM", "TPM", "DESeq" or "limma" |

Value

A normalized gene expression matrix.

Examples

```
data(testEQTL)
eqtl <- normalizeGene(testEQTL, method = "logNormalize")
```

| | |
|------------------|---|
| plots_theme_opts | <i>Theme options for customized plots</i> |
|------------------|---|

Description

Theme options for customized plots

Usage

```
plots_theme_opts()
```

Value

A ggplot2 theme object with customized settings.

Examples

```
library(ggplot2)
data <- data.frame(
  x = c("A", "B", "C", "D", "E"),
  y = c(10, 20, 30, 40, 50))
ggplot(data, aes(x, y)) +
  geom_point() +
  plots_theme_opts()
```

| | |
|--------------|--|
| poissonModel | <i>Poisson model fitting the gene expression matrix and genotype matrix.</i> |
|--------------|--|

Description

Poisson model fitting the gene expression matrix and genotype matrix.

Usage

```
poissonModel(
  eQTLObject,
  geneIDs,
  snpIDs,
  biClassify = FALSE,
  pAdjustMethod = "bonferroni",
  pAdjustThreshold = 0.05,
  logfcThreshold = 0.1
)
```

Arguments

| | |
|------------------|--|
| eQTLObject | An S4 object of class eQTLObject. |
| geneIDs | Matching genes can be used to fit data. |
| snpIDs | Matching SNPs can be used to fit data. |
| biClassify | The user chooses whether to convert the counting method of the snpMatrix to 0/1/2, TRUE indicates conversion, and FALSE indicates no conversion, default is FALSE. |
| pAdjustMethod | Methods for p-value adjusting, one of "bonferroni", "holm", "hochberg", "hommel" or "BH". The default option is "bonferroni". |
| pAdjustThreshold | Only SNP-Gene pairs with adjusted p-values meeting the threshold will be displayed. The default value is 0.05. |
| logfcThreshold | Represents the minimum beta threshold for fitting SNP-Gene pairs. |

Value

Dataframe that contains gene-SNP pairs' information.

Examples

```
data(testEQTL)
Gene <- rownames(slot(testEQTL, "filterData")$expMat)
SNP <- rownames(slot(testEQTL, "filterData")$snpMat)
poissonResult <- poissonModel(
  eQTLObject = testEQTL,
  geneIDs = Gene,
  snpIDs = SNP,
  biClassify = FALSE,
  pAdjustMethod = "bonferroni",
  pAdjustThreshold = 0.05,
  logfcThreshold = 0.025
)
```

| | |
|----------------|---|
| process_matrix | <i>Process a matrix to extract a row and convert it to a data frame</i> |
|----------------|---|

Description

Process a matrix to extract a row and convert it to a data frame

Usage

```
process_matrix(id, matrix, name)
```

Arguments

| | |
|--------|---|
| id | The identifier for the row to be extracted from the matrix. |
| matrix | The input matrix from which the row will be extracted. |
| name | The column names for the resulting data frame. |

Value

A data frame containing the extracted row and a column with the row names.

Examples

```
rownames <- c("CNN2", "TIGD2", "DTD2")
colnames <- c("Col1", "Col2", "Col3", "Col4")
matrix_data <- matrix(1:12, nrow = 3, ncol = 4,
  dimnames = list(rownames, colnames))
geneid <- "CNN2"
gene_mat <- process_matrix(geneid, matrix_data, "gene_mat")
```

| | |
|-----------------|--|
| remove_outliers | <i>Remove outliers from gene expression data and update cell lists</i> |
|-----------------|--|

Description

remove_outliers() is a function designed to process gene expression data stored in an expression matrix. It identifies outliers within the data based on the MAD method and filters them out. The function updates specified cell lists by retaining only those cells that have non-outlier expression values for a specified gene.

Usage

```
remove_outliers(exprsMat, Geneid, A_cells, B_cells, C_cells = NULL)
```

Arguments

| | |
|----------|------------------------------|
| exprsMat | Input gene expression matrix |
| Geneid | Chosen gene id. |
| A_cells | A genotype cells |
| B_cells | B genotype cells |
| C_cells | C genotype cells |

Value

a list of cells ids

Examples

```
## Mock expression matrix
set.seed(123)
exprsMat <- matrix(rnorm(200), nrow = 5)
rownames(exprsMat) <- paste0("Gene", 1:nrow(exprsMat))
colnames(exprsMat) <- paste0("cell", 1:ncol(exprsMat))
A_cells <- colnames(exprsMat)[1:13] # Example A cell list
B_cells <- colnames(exprsMat)[14:26] # Example B cell list
C_cells <- colnames(exprsMat)[27:40] # Example C cell list
remove_outliers(exprsMat, "Gene1", A_cells, B_cells, C_cells)
```

| | |
|-----------------|--|
| set_filter_data | <i>Generic to set eQTLObject filter data</i> |
|-----------------|--|

Description

Generic to set eQTLObject filter data

Usage

```
set_filter_data(x, value, name)
```

Arguments

| | |
|-------|--|
| x | A eQTLObject object. |
| value | The filtered data. |
| name | The matrix named 'name' is stored under the 'filterData' slot as an element within its list. |

Value

eQTLObject.

Examples

```
data(testEQTL)
data123 <- matrix(0, nrow = 3, ncol = 3)
set_filter_data(testEQTL, data123, "expMat")
```

set_filter_data,eQTLOBJECT-method

Method to set eQTLOBJECT filter data

Description

Method to set eQTLOBJECT filter data

Usage

```
## S4 method for signature 'eQTLOBJECT'
set_filter_data(x, value, name)
```

Arguments

| | |
|-------|--|
| x | A eQTLOBJECT object. |
| value | The filtered data. |
| name | The matrix named 'name' is stored under the 'filterData' slot as an element within its list. |

Value

eQTLOBJECT.

Examples

```
data(testEQTL)
data123 <- matrix(0, nrow = 3, ncol = 3)
set_filter_data(testEQTL, data123, "expMat")
```

set_model_info *Generic to set eQTLObject used model information*

Description

Generic to set eQTLObject used model information

Usage

```
set_model_info(x, value)
```

Arguments

x A eQTLObject object.
value The used model information to set to eQTLObject.

Value

eQTLObject.

Examples

```
data(testEQTL)
useModel <- "zinb"
set_model_info(testEQTL, useModel)
```

set_model_info,eQTLObject-method
Method to set eQTLObject used model information

Description

Method to set eQTLObject used model information

Usage

```
## S4 method for signature 'eQTLObject'
set_model_info(x, value)
```

Arguments

x A eQTLObject object.
value The used model information to set to eQTLObject.

Value

eQTLObject.

Examples

```
data(testEQTL)
useModel <- "zinb"
set_model_info(testEQTL, useModel)
```

| | |
|--------------|---|
| set_raw_data | <i>Generic to set eQTLObject raw data</i> |
|--------------|---|

Description

Generic to set eQTLObject raw data

Usage

```
set_raw_data(x, value, name)
```

Arguments

| | |
|-------|---|
| x | A eQTLObject object. |
| value | The raw data. |
| name | The matrix named 'name' is stored under the 'rawData' slot as an element within its list. |

Value

eQTLObject.

Examples

```
data(testEQTL)
data123 <- matrix(0, nrow = 3, ncol = 3)
set_raw_data(testEQTL, data123, "rawExpMat")
```

set_raw_data, eQTLObject-method
Method to set eQTLObject raw data

Description

Method to set eQTLObject raw data

Usage

```
## S4 method for signature 'eQTLObject'  
set_raw_data(x, value, name)
```

Arguments

| | |
|-------|---|
| x | A eQTLObject object. |
| value | The raw data. |
| name | The matrix named 'name' is stored under the 'rawData' slot as an element within its list. |

Value

eQTLObject.

Examples

```
data(testEQTL)  
data123 <- matrix(0, nrow = 3, ncol = 3)  
set_raw_data(testEQTL, data123, "rawExpMat")
```

set_result_info *Generic to set the result of identifying eQTLs from scRNA-seq data*

Description

Generic to set the result of identifying eQTLs from scRNA-seq data

Usage

```
set_result_info(x, value)
```

Arguments

| | |
|-------|---|
| x | A eQTLObject object. |
| value | A dataframe, each row describes eQTL discovering result of a SNP-Gene pair. |

Value

eQTLObject.

Examples

```
data(testEQTl)
result <- matrix(0, nrow = 3, ncol = 3)
set_result_info(testEQTl, result)
```

set_result_info,eQTLObject-method

Method to set the result of identifying eQTLs from scRNA-seq data

Description

Method to set the result of identifying eQTLs from scRNA-seq data

Usage

```
## S4 method for signature 'eQTLObject'
set_result_info(x, value)
```

Arguments

| | |
|-------|---|
| x | A eQTLObject object. |
| value | A dataframe, each row describes eQTL discovering result of a SNP-Gene pair. |

Value

eQTLObject.

Examples

```
data(testEQTl)
result <- matrix(0, nrow = 3, ncol = 3)
set_result_info(testEQTl, result)
```

```
show, eQTLObjct-method
```

Show Method for eQTLObjct Class

Description

This method is to display information about an object of class eQTLObjct. When called on an eQTLObjct, it prints a descriptive message to the console

Usage

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

Arguments

object An S4 object of class eQTLObjct.

Value

information of eQTLObjct

Examples

```
data(testEQTL)
testEQTL
```

```
testEQTL
```

Test eqtl object

Description

An 'eqtlObject' created by the 'createQTLObjct' function, where the raw expression matrix is normalized using 'normalizeGene()', and both the genotype matrix and the normalized gene expression matrix are filtered by 'filterGeneSNP()'.
 testEQTL.rds is the RDS format versions of the original testEQTL.rda, providing the same normalized eQTL object for easier loading and use in R.

Usage

```
data(testEQTL)

data(testEQTL)
```

Format

A simple object.

A eqtlObject read by the 'readRDS' function.

Examples

```
data(testEQTL)
data(testEQTL)
```

| | |
|----------|-------------------------------------|
| testGene | <i>Test Gene Expression Dataset</i> |
|----------|-------------------------------------|

Description

A dataset containing example gene expression data for testing purposes. 100 rows and 2705 columns. The row names represent gene IDs or SYMBOL and the column names represent cell IDs.

Usage

```
data(testGene)
```

Format

A simple matrix.

Examples

```
data(testGene)
```

| | |
|------------|--------------------------|
| testSeurat | <i>Test SeuratObject</i> |
|------------|--------------------------|

Description

A Seurat object for single-cell RNA-seq data.

testSeurat.rds datasets are the RDS format versions of the original testSeurat.rda files, providing the preprocessed Seurat object for easier loading and use in R.

Usage

```
data(testSeurat)
```

```
data(testSeurat)
```

Format

A object
A Seurat read by the 'readRDS' function.

Examples

```
data(testSeurat)
data(testSeurat)
```

| | |
|---------|------------------------------|
| testSNP | <i>Test Genotype Dataset</i> |
|---------|------------------------------|

Description

A dataset containing single nucleotide variant data. 1000 rows and 2705 columns. Each row is one variant and each column is one cell.

Usage

```
data(testSNP)
```

Format

A simple matrix.

Examples

```
data(testSNP)
```

| | |
|----------|------------------------------|
| testSNP2 | <i>Test Genotype Dataset</i> |
|----------|------------------------------|

Description

A dataset containing single nucleotide variant data. 500 rows and 500 columns. Each row is one variant and each column is one cell.

Usage

```
data(testSNP2)
```

Format

A simple matrix.

Examples

```
data(testSNP2)
```

| | |
|---------------|--|
| TPM_normalize | <i>Normalize the gene expression matrix with TPM</i> |
|---------------|--|

Description

'TPM_normalize()' scales an expression matrix using Transcripts Per Million (TPM) normalization, applying logarithm and scaling operations to adjust data based on library size.

Usage

```
TPM_normalize(expressionMatrix)
```

Arguments

expressionMatrix
Input raw gene expression matrix.

Value

A gene expression matrix after normalized.

Examples

```
data(testGene)  
TPM_normalize(testGene)
```

| | |
|--------------|---|
| visualizeQTL | <i>visualizeQTL: Visualize the gene-snp pairs by group.</i> |
|--------------|---|

Description

visualizeQTL: Visualize the gene-snp pairs by group.

Usage

```
visualizeQTL(  
  eQTLObject,  
  SNPid,  
  Geneid,  
  groupName = NULL,  
  plotype = "QTLplot",  
  removeoutlier = FALSE  
)
```

Arguments

| | |
|---------------|---|
| eQTLObject | An S4 object of class eQTLObject. |
| SNPid | ID of SNP. |
| Geneid | ID of Gene. |
| groupName | Users can choose one or more than one single cell groups. |
| plottype | Types of plot, one of "QTLplot", "violin", "boxplot" or "histplot". |
| removeoutlier | Whether identify and remove the outliers. Default by FALSE. |

Value

list

Examples

```
data(testEQL)
## We have to call the eQTLs firstly using `callQTL()`.
eqtl <- callQTL(eQTLObject = testEQL, useModel = "linear")
visualizeQTL(eQTLObject = eqtl,
SNPid = "1:632647",
Geneid = "RPS27",
groupName = NULL,
plottype = "QTLplot",
removeoutlier = FALSE)
```

zinbModel

Zinb model fitting the gene expression matrix.

Description

Zinb model fitting the gene expression matrix.

Usage

```
zinbModel(
  eQTLObject,
  geneIDs,
  snpIDs,
  biClassify = FALSE,
  pAdjustMethod = "bonferroni",
  pAdjustThreshold = 0.05
)
```

Arguments

| | |
|------------------|--|
| eQTLObject | An S4 object of class eQTLObject. |
| geneIDs | Matching genes can be used to fit data. |
| snpIDs | Matching SNPs can be used to fit data. |
| biClassify | The user chooses whether to convert the counting method of the snpMatrix to 0/1/2, TRUE indicates conversion, and FALSE indicates no conversion, default is no conversion. |
| pAdjustMethod | Methods for p-value adjusting, one of 'bonferroni', 'holm', 'hochberg', 'holmel' or 'BH'. The default option is 'bonferroni'. |
| pAdjustThreshold | Only SNP-Gene pairs with adjusted p-values meeting the threshold will be displayed. Default by 0.05. |

Value

Dataframe that contains gene-SNP pairs' information.

Examples

```
data(testEQTL)
Gene <- rownames(slot(testEQTL, 'filterData')$expMat)
SNP <- rownames(slot(testEQTL, 'filterData')$snpMat)
zinbResult <- zinbModel(
  eQTLObject = testEQTL,
  geneIDs = Gene,
  snpIDs = SNP,
  biClassify = FALSE,
  pAdjustMethod = 'bonferroni',
  pAdjustThreshold = 0.05)
```

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