

Package ‘rqt’

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Type Package

Title rqt: utilities for gene-level meta-analysis

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Description Despite the recent advances of modern GWAS methods, it still remains an important problem of addressing calculation an effect size and corresponding p-value for the whole gene rather than for single variant. The R- package rqt offers gene-level GWAS meta-analysis. For more information, see: ``Gene-set association tests for next-generation sequencing data" by Lee et al (2016), *Bioinformatics*, 32(17), i611-i619, <doi:10.1093/bioinformatics/btw429>.

URL <https://github.com/izhbannikov/rqt>

BugReports <https://github.com/izhbannikov/rqt/issues>

License GPL

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R topics documented:

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| | |
|------------------|---|
| build.null.model | <i>Applies linear of logistic regression to the data.</i> |
|------------------|---|

Description

Applies linear of logistic regression to the data.

Usage

```
build.null.model(y, x, reg.family = "binomial", verbose = FALSE)
```

Arguments

| | |
|------------|--|
| y | A vector with values of dependent variable (outcome). |
| x | A data.frame of covariates. |
| reg.family | A regression family. Can be either "binomial" or "gaussian." |
| verbose | Indicates verbosing output. Default: FALSE. |

Value

A list of two: "S" - a dataframe with predictors and "fit" - an object returned by "glm" function.

| | |
|------------|---|
| covariates | <i>This function performs an access to covariates</i> |
|------------|---|

Description

This function performs an access to covariates

An accessor to covariates

Usage

```
covariates(obj)

## S4 method for signature 'rqt'
covariates(obj)
```

Arguments

obj An object of rqt class.

Value

covariates returns the covariates

Examples

```
data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
covariates(obj)
```

| | |
|----------|---|
| geneTest | <i>This function performs a gene-level test based on combined effect sizes.</i> |
|----------|---|

Description

This function performs a gene-level test based on combined effect sizes.

geneTest This function performs a gene-level test based on combined effect sizes.

Usage

```
geneTest(obj, ...)

## S4 method for signature 'rqt'
geneTest(obj, perm = 0, STT = 0.2, weight = FALSE,
  cumvar.threshold = 75, out.type = "D", method = "pca",
  scaleData = FALSE, asym.pval = FALSE, penalty = 0.001,
  verbose = FALSE)
```

Arguments

| | |
|------------------|---|
| obj | Object of class rqt |
| ... | Additional parameters to pass to the function |
| perm | Integer indicating the number of permutations to compute p-values. Default: 0. |
| STT | Numeric indicating soft truncation threshold (STT) to convert to gamma parameter (must be ≤ 0.4). Needed for an optimal parameter a in Gamma-distribution. Default: 0.2. See, for example, Fridley, et al 2013: "Soft truncation thresholding for gene set analysis of RNA-seq data: Application to a vaccine study". |
| weight | Logical value. Indicates using weights (see Lee et al 2016). Default: FALSE. |
| cumvar.threshold | Numeric value indicating the explained variance threshold for PCA-like methods. Default: 75 |
| out.type | Character, indicating a type of phenotype. Possible values: D (dichotomous or binary), C (continuous or quantitative). |
| method | Method used to reduce multicollinearity and account for LD. Default: pca. Another methods available: lasso, ridge, pls. |
| scaleData | A logic parameter (TRUE/FALSE) indicating scaling of the genotype dataset. |
| asym.pval | Indicates Monte Carlo approximation for p-values. Default: FALSE. |
| penalty | A value of penalty parameter for LASSO/ridge regression. Default: 0.001 |
| verbose | Indicates verbosing output. Default: FALSE. |

Value

Updated rqt object with result slot

Examples

```
data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
  package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
res <- geneTest(obj, method="pca", out.type = "D")
print(res)
```

| | |
|--------------|--|
| geneTestMeta | <i>This function performs a gene-level meta-analysis based on combined effect sizes.</i> |
|--------------|--|

Description

This function performs a gene-level meta-analysis based on combined effect sizes.

This function performs a gene-level meta-analysis based on combined effect sizes.

Usage

```
geneTestMeta(objects, ...)
```

```
## S4 method for signature 'list'
geneTestMeta(objects, perm = 0, STT = 0.2,
  weight = FALSE, cumvar.threshold = 75, out.type = "D", method = "pca",
  scaleData = FALSE, asym.pval = FALSE, comb.test = "wilkinson",
  penalty = 0.001, verbose = FALSE)
```

Arguments

| | |
|------------------|---|
| objects | List of objects of class rqt |
| ... | Additional parameters to pass to the function |
| perm | Integer indicating the number of permutations to compute p-values. Default: 0. |
| STT | Numeric indicating soft truncation threshold (STT) to convert to gamma parameter (must be ≤ 0.4). Needed for an optimal parameter a in Gamma-distribution. Default: 0.2. See, for example, Fridley, et al 2013: "Soft truncation thresholding for gene set analysis of RNA-seq data: Application to a vaccine study". |
| weight | Logical value. Indicates using weights (see Lee et al 2016). Default: FALSE. |
| cumvar.threshold | Numeric value indicating the explained variance threshold for PCA-like methods. Default: 75 |
| out.type | Character, indicating a type of phenotype. Possible values: D (dichotomous or binary), C (continuous or quantitative). |
| method | Method used to reduce multicollinearity and account for LD. Default: pca. Other methods available: lasso, ridge, pls. |
| scaleData | A logic parameter (TRUE/FALSE) indicating scaling of the genotype dataset. |
| asym.pval | Indicates Monte Carlo approximation for p-values. Default: FALSE. |
| comb.test | Statistical test for combining p-values. |
| penalty | Value of penalty parameter for LASSO/ridge regression. Default: 0.001 |
| verbose | Indicates verbosing output. Default: FALSE. |

Value

A list of two: (i) final.pvalue - a final p-value across all studies; (ii) pvalueList - p-values for each study;

A list of two: (i) final.pvalue - a final p-value across all studies; (ii) pvalueList - p-values for each study;

Examples

```
data1 <- data.matrix(read.table(system.file("extdata/phengen2.dat",
                                         package="rqt"), skip=1))

pheno <- data1[,1]
geno <- data1[, 2:dim(data1)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj1 <- rqt(phenotype=pheno, genotype=geno.obj)

data2 <- data.matrix(read.table(system.file("extdata/phengen3.dat",
                                         package="rqt"), skip=1))

pheno <- data2[,1]
geno <- data2[, 2:dim(data2)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj2 <- rqt(phenotype=pheno, genotype=geno.obj)

data3 <- data.matrix(read.table(system.file("extdata/phengen.dat",
                                         package="rqt"), skip=1))

pheno <- data3[,1]
geno <- data3[, 2:dim(data3)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj3 <- rqt(phenotype=pheno, genotype=geno.obj)

res.meta <- geneTestMeta(list(obj1, obj2, obj3))
print(res.meta)
```

genotype

This function performs an access to genotype.

Description

This function performs an access to genotype.

A genotype accessor

Usage

```
genotype(obj)
```

```
## S4 method for signature 'rqt'
genotype(obj)
```

Arguments

obj An object of rqt class.

Value

genotype returns the genotype

Examples

```
data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
genotype(obj)
```

get.a

Get a given STT

Description

Get a given STT

Usage

```
get.a(L, STT = 0.2)
```

Arguments

L TODO

STT Numeric indicating soft truncation threshold (STT) to convert to gamma parameter (must be ≤ 0.4).

Value

a TODO

| | |
|-----------|--|
| phenotype | <i>This function performs an access to phenotype</i> |
|-----------|--|

Description

This function performs an access to phenotype
A phenotype accessor

Usage

```
phenotype(obj)

## S4 method for signature 'rqt'
phenotype(obj)
```

Arguments

obj An object of rqt class.

Value

phenotype returns the phenotype

Examples

```
data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
phenotype(obj)
```

| | |
|------------|---|
| preprocess | <i>Preprocess input data with Principal Component Analysis method (PCA)</i> |
|------------|---|

Description

Preprocess input data with Principal Component Analysis method (PCA)

Usage

```
preprocess(data, pheno = NULL, method = "pca", reg.family = "binomial",
scaleData = FALSE, cumvar.threshold = 75, out.type = "D",
penalty = 0.001, verbose = FALSE)
```


Arguments

| | |
|------------------|---|
| data | An input matrix with values of independent variables (predictors). |
| pheno | A phenotype - column-vector, needed for LASSO/ridge and NULL by default. |
| method | A dimensionality reduction method. Default: pca. |
| reg.family | A regression family. Default: "binomial". |
| scaledata | A logical variable, indicates whether or not scaling should be performed. Default: FALSE. |
| cumvar.threshold | A threshold value for explained variance. Default: 75 |
| out.type | An output (phenotype) type. Default: "D" |
| penalty | Value of penalty parameter for LASSO/ridge regression. Default: 0.001 |
| verbose | Indicates verbosing output. Default: FALSE. |

Value

A list of one: "S" - a data frame of predictor values.

| | |
|---------|---|
| results | <i>This function performs an access to covariates</i> |
|---------|---|

Description

This function performs an access to covariates

An accessor to results

Usage

```
results(obj)
```

```
## S4 method for signature 'rqt'
results(obj)
```

Arguments

| | |
|-----|-------------------------|
| obj | An object of rqt class. |
|-----|-------------------------|

Value

results returns the results

Examples

```

data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
res <- geneTest(obj, method="pca", out.type = "D")
results(res)

```

rqt

*The rqt class constructor***Description**

This function generates rqt class objects

Usage

```

rqt(phenotype = NULL, genotype = NULL, covariates = NULL,
    results = NULL)

```

Arguments

| | |
|------------|--|
| phenotype | Phenotype (a vector of length N, where N - number of individuals). |
| genotype | Genotype - an object of class SummarizedExperiment. Should contain one assay (matrix, N by M where N - number of individuals, M - number of genetic variants). |
| covariates | Covariates, a data frame N by K where N - number of individuals, K - number of covariates |
| results | A list of two: test statistics: (Q1, Q2, Q3), p-values: (p1 .Q1, p2 .Q2, p3 .Q3) |

Value

Object of class rqt

Examples

```

data <- data.matrix(read.table(system.file("extdata/test.bin1.dat",
package="rqt"), header=TRUE))
pheno <- data[,1]
geno <- data[, 2:dim(data)[2]]
colnames(geno) <- paste(seq(1, dim(geno)[2]))
geno.obj <- SummarizedExperiment(geno)
obj <- rqt(phenotype=pheno, genotype=geno.obj)
print(obj)

```

| | |
|-----------|----------------------|
| rqt-class | <i>The rqt class</i> |
|-----------|----------------------|

Description

This class stores parameters and results of the rqt algorithms

Slots

phenotype: Phenotype (a vector of length N, where N - number of individuals).

genotype: Genotype - an object of class SummarizedExperiment. Should contain one assay (matrix, N by M where N - number of individuals, M - number of genetic variants).

covariates: data frame N by K where N - number of individuals, K - number of covariates)

results: A list of two: test statistics (Q1, Q2, Q3), p-values (p1.Q1, p2.Q2, p3.Q3)

| | |
|-------------|---|
| rqt-general | <i>General functions of rqt such as accessors and printing.</i> |
|-------------|---|

Description

Common methods for class rqt. This document lists a series of basic methods for the class rqt

Details

Common methods for class rqt

| | |
|---------------------|---|
| simple.multivar.reg | <i>Applies linear of logistic regression to the data.</i> |
|---------------------|---|

Description

Applies linear of logistic regression to the data.

Usage

```
simple.multivar.reg(null.model, Z, verbose = FALSE)
```

Arguments

null.model A fitted null model

Z A genotype matrix

verbose Indicates verbosing output. Default: FALSE.

Value

A list of two: "S" - a dataframe with predictors and "fit" - an object returned by "glm" function.

| | |
|------------|--|
| vcov_ridge | <i>vcov_ridge: returns variance-covariance matrix and standard deviation for ridge/LASSO regression object</i> |
|------------|--|

Description

vcov_ridge: returns variance-covariance matrix and standard deviation for ridge/LASSO regression object

Usage

```
vcov_ridge(x, y, rmod, verbose = FALSE)
```

Arguments

| | |
|---------|---|
| x | Genotype matrix |
| y | Phenotype |
| rmod | Ridge/LASSO regression object |
| verbose | Indicates verbosing output, Default: FALSE. |

Value

list(vcov, se). vcov: variance-covariance matrix; se: standard deviation

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