

Package ‘rqt’

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Type Package

Title rqt: utilities for gene-level meta-analysis

Version 1.34.0

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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Suggests BiocStyle, knitr, rmarkdown

VignetteBuilder knitr

Imports stats,Matrix,ropls,methods,car,RUnit,metap,CompQuadForm,glmnet,utils,pls

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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

This function performs an access to covariates

Description

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

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

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. 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.
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
 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(pheno=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)

```

geneTestOne

get.reg.family

Description

get.reg.family

Usage

```

geneTestOne(
  phenotype,
  genotype,
  covariates,
  STT = 0.2,
  weight = FALSE,
  cumvar.threshold = 75,
  method = "pca",
  out.type = "D",
  scaleData = FALSE,
  penalty = 0.001,
  verbose = FALSE
)

```

Arguments

phenotype	phenotype
genotype	genotype
covariates	covariates
STT	STT
weight	weight
cumvar.threshold	cumvar.threshold
method	method
out.type	out.type
scaleData	scaleData
penalty	penalty
verbose	verbose

Value

rslt

genotype	<i>This function performs an access to genotype.</i>
----------	--

Description

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(pheno=pheno, genotype=geno.obj)
genotype(obj)
```

get.a	<i>Get a given STT</i>
-------	------------------------

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 number from gamma distribution

get.reg.family	<i>get.reg.family</i>
----------------	-----------------------

Description

get.reg.family

Usage

get.reg.family(out.type = "D")

Arguments

out.type	out.type
----------	----------

Value

reg.family

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

Description

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 wheither or not scaling should be performed. Default: FALSE.
cumvar.threshold	A threshold value for explained variance. Default: 75

<code>out.type</code>	An output (phenotype) type. Default: "D"
<code>penalty</code>	Value of penalty parameter for LASSO/ridge regression. Default: 0.001
<code>verbose</code>	Indicates verbosing output. Default: FALSE.

Value

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

<code>preprocessLASSO</code>	<i>preprocessLASSO</i>
------------------------------	------------------------

Description

`preprocessLASSO`

Usage

`preprocessLASSO(data, pheno, reg.family, penalty = 0.001)`

Arguments

<code>data</code>	data
<code>pheno</code>	pheno data
<code>reg.family</code>	reg.family
<code>penalty</code>	penalty Default: FALSE.

Value

`list(S, fit, model)`

<code>preprocessPCA</code>	<i>preprocessPCA</i>
----------------------------	----------------------

Description

`preprocessPCA`

Usage

`preprocessPCA(data, scaleData, cumvar.threshold, verbose)`

Arguments

data	data
scaleData	scaled data
cumvar.threshold	cumvar.threshold
verbose	Indicates verbosing output Default: FALSE.

Value

list(S, indices, model).

preprocessPLS	<i>preprocessPLS</i>
---------------	----------------------

Description

preprocessPLS

Usage

preprocessPLS(data, pheno, scaleData, cumvar.threshold, out.type)

Arguments

data	data
pheno	pheno data
scaleData	scaleData
cumvar.threshold	cumvar.threshold
out.type	out.type Default: FALSE.

Value

list(S, Y, model)

preprocessRidge	<i>preprocessLASSO</i>
-----------------	------------------------

Description

preprocessLASSO

Usage

```
preprocessRidge(data, pheno, reg.family, penalty = 0.001)
```

Arguments

data	data
pheno	pheno data
reg.family	reg.family
penalty	penalty Default: FALSE.

Value

list(S, fit, model)

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

Description

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(pheno=pheno, genotype=geno.obj)
res <- geneTest(obj, method="pca", out.type = "D")
results(res)
```

ridge_se*Importing required packages and functions*

Description

Importing required packages and functions

Usage

```
ridge_se(xs, y, yhat, my_mod, verbose = FALSE)
```

Arguments

xs	Genotype matrix
y	Phenotype
yhat	Ridge/LASSO regression object
my_mod	Ridge/LASSO regression object
verbose	Indicates verbosing output, Default: FALSE.

Value

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

rqt*The rqt class constructor*

Description

This function generates rqt class objects

Usage

```
rqt(pheno = 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

The rqt class

Description

This class stores parameters and results of the rtq algorithms

Value

None

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`*General functions of rqt such as accessors and printing.*

Description

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

Details

Common methods for class rqt

Value

None

`simple.multvar.reg`*Applies linear of logistic regression to the data.*

Description

Applies linear of logistic regression to the data.

Usage

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

Arguments

<code>null.model</code>	A fitted null model
<code>Z</code>	A genotype matrix
<code>verbose</code>	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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