

Package ‘rqt’

September 25, 2024

Type Package

Title rqt: utilities for gene-level meta-analysis

Version 1.31.1

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

RoxygenNote 7.3.2

Suggests BiocStyle, knitr, rmarkdown

VignetteBuilder knitr

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

Depends R (>= 3.4), SummarizedExperiment

Encoding UTF-8

biocViews GenomeWideAssociation, Regression, Survival, PrincipalComponent, StatisticalMethod, Sequencing

git_url <https://git.bioconductor.org/packages/rqt>

git_branch devel

git_last_commit 107d3bf

git_last_commit_date 2024-08-01

Repository Bioconductor 3.20

Date/Publication 2024-09-24

Author Ilya Zhbannikov [aut, cre],
Konstantin Arbeev [aut],
Anatoliy Yashin [aut]

Maintainer Ilya Zhbannikov <ilya.zhbannikov@duke.edu>

Contents

build.null.model	2
covariates	3
geneTest	3
geneTestMeta	5
geneTestOne	6
genotype	7
get.a	8
get.reg.family	9
phenotype	9
preprocess	10
preprocessLASSO	11
preprocessPCA	11
preprocessPLS	12
preprocessRidge	12
results	13
ridge_se	13
rqt	14
rqt-class	15
rqt-general	15
simple.multivar.reg	15
vcov_ridge	16
Index	17

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

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 <code>rqt</code>
...	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: <code>pca</code> . Other methods available: <code>lasso</code> , <code>ridge</code> , <code>pls</code> .
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(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)
```

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

This function performs an access to genotype.

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(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 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 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.

```
preprocessLASSO      preprocessLASSO
```

Description

preprocessLASSO

Usage

preprocessLASSO(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)

```
preprocessPCA      preprocessPCA
```

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      preprocessPLS
```

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   preprocessLASSO
```

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

ridge_se	<i>Importing required packages and functions</i>
----------	--

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(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 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	<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

Value

None

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

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.

<code>vcov_ridge</code>	<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

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

Value

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

Index

`build.null.model`, 2

`covariates`, 3
`covariates`, `rqt-method (covariates)`, 3

`geneTest`, 3
`geneTest`, `rqt-method (geneTest)`, 3
`geneTestMeta`, 5
`geneTestMeta`, `list-method (geneTestMeta)`, 5
`geneTestOne`, 6
`genotype`, 7
`genotype`, `rqt-method (genotype)`, 7
`get.a`, 8
`get.reg.family`, 9

`phenotype`, 9
`phenotype`, `rqt-method (phenotype)`, 9
`preprocess`, 10
`preprocessLASSO`, 11
`preprocessPCA`, 11
`preprocessPLS`, 12
`preprocessRidge`, 12
`print.rqt (rqt-general)`, 15

`results`, 13
`results`, `rqt-method (results)`, 13
`ridge_se`, 13
`rqt`, 14
`rqt-class`, 15
`rqt-general`, 15

`show.rqt (rqt-general)`, 15
`simple.multivar.reg`, 15
`summary.rqt (rqt-general)`, 15

`vcov_ridge`, 16