

# Package ‘rqt’

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**Type** Package

**Title** rqt: utilities for gene-level meta-analysis

**Version** 1.32.0

**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](https://doi.org/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

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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**

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 $\leq 0.4$ ). 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 <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 $\leq 0.4$ ). 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.
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  $\leq 0.4$ ).

**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
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

*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.multivar.reg

*Applies linear of logistic regression to the data.*


---

**Description**

Applies linear of logistic regression to the data.

**Usage**

```
simple.multivar.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

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