

# Package ‘rqt’

March 10, 2025

**Type** Package

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

**Version** 1.33.0

**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

**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** 4366457

**git\_last\_commit\_date** 2024-10-29

**Repository** Bioconductor 3.21

**Date/Publication** 2025-03-09

**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 . . . . .        | 7         |
| genotype . . . . .           | 8         |
| get.a . . . . .              | 8         |
| get.reg.family . . . . .     | 9         |
| phenotype . . . . .          | 9         |
| preprocess . . . . .         | 10        |
| preprocessLASSO . . . . .    | 11        |
| preprocessPCA . . . . .      | 11        |
| preprocessPLS . . . . .      | 12        |
| preprocessRidge . . . . .    | 13        |
| results . . . . .            | 13        |
| ridge_se . . . . .           | 14        |
| rqt . . . . .                | 14        |
| rqt-class . . . . .          | 15        |
| rqt-general . . . . .        | 16        |
| simple.multvar.reg . . . . . | 16        |
| vcov_ridge . . . . .         | 17        |
| <b>Index</b>                 | <b>18</b> |

---

|                  |   |
|------------------|---|
| 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(pheno=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 $\leq 0.4$ ). 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: 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  
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 $\leq 0.4$ ). 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: 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(phenotype=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 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.

---

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

---

**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)`

---

|                            |                      |
|----------------------------|----------------------|
| <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      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      This function performs an access to covariates
```

---

**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***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(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.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**

|            |   |
|------------|---|
| 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

# 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`, 7  
`genotype`, 8  
`genotype`, `rqt-method (genotype)`, 8  
`get.a`, 8  
`get.reg.family`, 9

`phenotype`, 9  
`phenotype`, `rqt-method (phenotype)`, 9  
`preprocess`, 10  
`preprocessLASSO`, 11  
`preprocessPCA`, 11  
`preprocessPLS`, 12  
`preprocessRidge`, 13  
`print.rqt (rqt-general)`, 16

`results`, 13  
`results`, `rqt-method (results)`, 13  
`ridge_se`, 14  
`rqt`, 14  
`rqt-class`, 15  
`rqt-general`, 16

`show.rqt (rqt-general)`, 16  
`simple.multivar.reg`, 16  
`summary.rqt (rqt-general)`, 16

`vcov_ridge`, 17