

# Package ‘rqt’

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**Type** Package

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

**Version** 1.37.0

**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

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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(pheno=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**

|                               |                                                                                                                                                                                                                                                                                                                               |
|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <code>obj</code>              | Object of class <code>rqt</code>                                                                                                                                                                                                                                                                                              |
| <code>...</code>              | Additional parameters to pass to the function                                                                                                                                                                                                                                                                                 |
| <code>perm</code>             | Integer indicating the number of permutations to compute p-values. Default: 0.                                                                                                                                                                                                                                                |
| <code>STT</code>              | 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". |
| <code>weight</code>           | Logical value. Indicates using weights (see Lee et al 2016). Default: FALSE.                                                                                                                                                                                                                                                  |
| <code>cumvar.threshold</code> | Numeric value indicating the explained variance threshold for PCA-like methods. Default: 75                                                                                                                                                                                                                                   |
| <code>out.type</code>         | Character, indicating a type of phenotype. Possible values: D (dichotomous or binary), C (continuous or quantitative).                                                                                                                                                                                                        |
| <code>method</code>           | 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> .                                                                                                                                                 |
| <code>scaleData</code>        | A logic parameter (TRUE/FALSE) indicating scaling of the genotype dataset.                                                                                                                                                                                                                                                    |
| <code>asym.pval</code>        | Indicates Monte Carlo approximation for p-values. Default: FALSE.                                                                                                                                                                                                                                                             |
| <code>penalty</code>          | A value of penalty parameter for LASSO/ridge regression. Default: 0.001                                                                                                                                                                                                                                                       |
| <code>verbose</code>          | 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 $\leq 0.4$ ). 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(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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