

# Package ‘QTLExperiment’

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**Description** QTLExperiment defines an S4 class for storing and manipulating summary statistics from QTL mapping experiments in one or more states. It is based on the 'SummarizedExperiment' class and contains functions for creating, merging, and subsetting objects. 'QTLExperiment' also stores experiment metadata and has checks in place to ensure that transformations apply correctly.

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|          |                                               |
|----------|-----------------------------------------------|
| mockQTLE | <i>Mock data for the QTLExperiment object</i> |
|----------|-----------------------------------------------|

---

Description

Functions to create fake input data for QTLExperiments. Note that this data is generated simply, and does not have consistency between betas, errors and p-values. It is helpful to populate the slots of a QTLExperiment object and has expected properties of the betas, errors and p-values assays. Namely, betas are symmetric (specifically normally distributed), errors are non-negative, and p-values consist of a null and significant distribution. The significant effects make up 10 across states and tests.

Feature IDs are simulated by randomly selecting a feature from the list c("geneA", "geneB", "geneC") with replacement. Variant IDs are created by concatenating the string "snp" with a random number in the range 1000:100000. Row names combine the feature and variant IDs using a vertical line as the separator.

**Usage**

```
mockQTLE(nStates = 10, nQTL = 100, names = TRUE)

mockSummaryStats(nStates = 10, nQTL = 100, names = TRUE)

mockMASHR(nStates = 10, nQTL = 100)

mockMASHR_FIT(nStates = 10, nQTL = 100)
```

**Arguments**

|         |                                         |
|---------|-----------------------------------------|
| nStates | Number of states                        |
| nQTL    | Number of QTL associations              |
| names   | Logical to include column and row names |

**Value**

an object containing simulated data.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```
nStates <- 6
nQTL <- 40

# Mock QTLExperiment data

qtle <- mockQTLE(nStates, nQTL)
dim(qtle)

mock_summary_stats <- mockSummaryStats(nStates=nStates, nQTL=nQTL)
mock_summary_stats$betas
mock_summary_stats$errors
mock_summary_stats$pvalues

# Mock MASHR data

mockr_sim <- mockMASHR(nStates=nStates, nQTL=nQTL)
mockr_sim$B
mockr_sim$Bhat
mockr_sim$Shat
```

## Description

These are methods for getting or setting `assay(qtLe, i=X, ...)` where `qtLe` is a [QTLExperiment](#) object and `X` is the name of the method. For example, `betas` will get or set `X="betas"`.

## Value

For assays, returns the value stored in the requested [assay](#).

For `assays<-value`, the relevant slot of the [QTLExperiment](#) is updated.

## Available methods

Here `x` is a [QTLExperiment](#) object, `value` is a matrix-like object with the same dimensions as `x`, and `...` are further arguments passed to [assay](#) (for the getter) or [assay<-](#) (for the setter).

`betas(x, ...)`, `betas(x, ...) <- value`: Get or set a matrix of raw betas, i.e., QTL effect sizes.

`errors(x, ...)`, `errors(x, ...) <- value`: Get or set a matrix of raw beta standard errors.

`pvalues(x, ...)`, `pvalues(x, ...) <- value`: Get or set a matrix of raw significance scores (e.g. `pvals`, `qvals`)

`lfsrs(x, ...)`, `lfsrs(x, ...) <- value`: Get or set a matrix of local false sign rates.

## Author(s)

Christina B Azodi, Amelia Dunstone

## See Also

[assay](#) and [assay<-](#), for the wrapped methods.

## Examples

```
qtLe <- mockQTLE()
new_betas <- matrix(rnorm(nrow(qtLe)*ncol(qtLe)), ncol=ncol(qtLe))
row.names(new_betas) <- row.names(qtLe)
colnames(new_betas) <- colnames(qtLe)
betas(qtLe) <- new_betas
dim(betas(qtLe))
```

**Description**

Function to coerce a mashr object (class list or mashr) into a QTLe object.

**Usage**

```
mash2qtle(data, sep = NULL, rowData = NULL, verbose = FALSE)

.mashData_2_qtle(data)

.mashFit_2_qtle(data)
```

**Arguments**

|         |                                                                                                                                                                     |
|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| data    | A mashr object output from <code>mash_set_data()</code> or <code>mash()</code> from mashr.                                                                          |
| sep     | String separating the <code>feature_id</code> from the <code>variant_id</code> in the <code>row.names</code> of the mashr object                                    |
| rowData | if <code>feature_id</code> and <code>variant_id</code> are not in the <code>row.names</code> , a <code>rowData</code> matrix can be provided with this information. |
| verbose | Logical.                                                                                                                                                            |

**Value**

A [QTLExperiment](#) object.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```
nStates <- 6
nQTL <- 40
mashr_sim <- mockMASHR(nStates, nQTL)

qtle2 <- mash2qtle(
  mashr_sim,
  rowData=DataFrame(
    feature_id=row.names(mashr_sim$Bhat),
    variant_id=sample(seq_len(nQTL)))
dim(qtle2)
```

---

`qtlexperiment`*Modify and view the colData of a QTLEExperiment*

---

## Description

Methods for changing the `colData` of a QTLEExperiment.

## Usage

```
## S4 replacement method for signature 'QTLEExperiment,DataFrame'
colData(x) <- value

## S4 replacement method for signature 'QTLEExperiment,NULL'
colData(x) <- value
```

## Arguments

|                    |                                                                                                |
|--------------------|------------------------------------------------------------------------------------------------|
| <code>x</code>     | is a <a href="#">QTLEExperiment</a> object                                                     |
| <code>value</code> | is a matrix-like object with number of rows equal to the number of columns in <code>x</code> . |

## Details

The `state_id` column in the `colData` is protected, and operations ensure that this column is not removed from the `colData`.

## Value

For `colData`, a DFrame is returned. For `colData<-`, a modified [QTLEExperiment](#) object is returned with the updated `colData`.

## Author(s)

Christina B Azodi, Amelia Dunstone

## Examples

```
qtlexperiment <- mockQTLE()
colData(qtlexperiment)
dim(colData(qtlexperiment))

qtlexperiment$batch <- "batch1"
colData(qtlexperiment)

# The state_id column is protected
colData(qtlexperiment) <- NULL
colData(qtlexperiment)
```

## Description

An overview of methods to combine multiple [QTLExperiment](#) objects by row or column. These methods ensure that all data fields remain synchronized when states or associations are added or removed.

## Value

A [QTLExperiment](#) object.

## Combining

In the following examples, ... contains one or more [QTLExperiment](#) object.

`rbind(..., deparse.level=1)`: Returns a [QTLExperiment](#) object where all objects are combined row-wise. Metadata is combined as in `?rbind, SummarizedExperiment-method`. The `deparse.level` specifies how `row.names` are generated as described in `?rbind`.

`cbind(..., deparse.level=1)`: Returns a [QTLExperiment](#) object where all objects are combined column-wise. Metadata is combined as in `?cbind, SummarizedExperiment-method`. The `deparse.level` specifies how `colnames` are generated as described in `?cbind`.

## Author(s)

Christina B Azodi

## Examples

```
qt1e <- mockQTLE()
qt1e2 <- qt1e
feature_id(qt1e2) <- paste0("x", feature_id(qt1e2))
rbind(qt1e, qt1e2)

qt1e2 <- qt1e
state_id(qt1e2) <- paste0("x", state_id(qt1e2))
cbind(qt1e, qt1e2)
```

---

|           |                                                                  |
|-----------|------------------------------------------------------------------|
| QTLe-name | <i>Return the name of a <a href="#">QTLEperiment</a> object.</i> |
|-----------|------------------------------------------------------------------|

---

## Description

Returns the name of an object of class [QTLEperiment](#).

## Arguments

|        |                                                              |
|--------|--------------------------------------------------------------|
| object | A <a href="#">QTLEperiment</a> object.                       |
| value  | Any character-like object or NULL to remove existing labels. |

## Value

For `mainExpName(object)`, returns the name associated to object.

For `mainExpName(object) <- value`, the name of the object object is updated.

## Available methods

In the following code snippets, object is a [QTLEperiment](#) objects.

`mainExpName(object)`: Return the name assigned to object.

`mainExpName(object) <- value`: Change the name assigned to object to value.

`mainExpName(object) <- NULL`: Remove the name associated to object.

## Author(s)

Christina B. Azodi

## See Also

[QTLEperiment](#), for the underlying class definition.

## Examples

```
qtle <- mockQTLE()
mainExpName(qtle)
mainExpName(qtle) <- "test_name"
mainExpName(qtle)
```

---

|              |                                  |
|--------------|----------------------------------|
| QTLe-recover | <i>Recover QTLExperiment IDs</i> |
|--------------|----------------------------------|

---

**Description**

Function to recover protected rowData (feature\_id, variant\_id) and colData (state\_id) from internal structure.

**Usage**

```
.recover_qtle_ids(object)
```

**Arguments**

object                    QTLExperiment object

**Value**

A [QTLExperiment](#) object with recovered rowData or colData.

---

|              |                                         |
|--------------|-----------------------------------------|
| qtle-rowData | <i>rowData method for QTLExperiment</i> |
|--------------|-----------------------------------------|

---

**Description**

Methods for changing the [rowData](#) of a QTLExperiment.

**Usage**

```
## S4 method for signature 'QTLExperiment'
rowData(x, use.names = TRUE)

## S4 replacement method for signature 'QTLExperiment,DataFrame'
rowData(x) <- value

## S4 replacement method for signature 'QTLExperiment,NULL'
rowData(x) <- value
```

**Arguments**

x                    is a [QTLExperiment](#) object

use.names           is a logical specifying whether or not to propagate the rownames of x to the returned DFrame object.

value                is a matrix-like object with number of rows equal to the number of rows in x.

**Details**

The `feature_id` and `variant_id` columns in the `rowData` are protected, and operations ensure that these columns are preserved in the `rowData`.

**Value**

For `rowData`, a `DFrame` is returned. For `rowData<-`, a modified `QTLEExperiment` object is returned with the updated `rowData`.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```
qtlexperiment <- mockQTLE()
rowData(qtlexperiment)
dim(rowData(qtlexperiment))

rowData(qtlexperiment)$chr <- ifelse(feature_id(qtlexperiment) %in% c("geneA", "geneB"), "chr1", "chr2")
rowData(qtlexperiment)

# The state_id column is protected
rowData(qtlexperiment) <- NULL
rowData(qtlexperiment)
```

---

qtlexperiment

*Named rowData getters and setters*


---

**Description**

These are methods for getting or setting protected `rowData` columns (i.e. `feature_id` and `variant_id`).

**Arguments**

|                     |                                                                         |
|---------------------|-------------------------------------------------------------------------|
| <code>object</code> | is a <code>QTLEExperiment</code> object.                                |
| <code>value</code>  | is a vector with length equal to the number of rows of <code>x</code> . |

**Details**

QTL are associations between a genetic variants and a quantitative feature. The `feature_id` and `variant_id` methods can be used to get or set feature IDs and variant IDs, respectively, across a `QTLEExperiment` object. The values are stored in the `rowData` compartments and have additional protections to prevent them being removed or overwritten. The `feature_id` can store gene or metabolite names, while `variant_id` could be used to store variant information such as SNP names.

## Value

For `feature_id`, a vector is returned containing the name of the feature tested in each association. For `feature_id<-`, a modified object is returned with the updated `feature_ids` in `rowData`, and in the `row.names` of the `QTLEExperiment` object. For `variant_id`, a vector is returned containing the name of the variant tested in each association. For `variant_id<-`, a modified object is returned with the updated `variant_ids` in `rowData`, and in the `row.names` of the `QTLEExperiment` object.

## Available methods

Here `object` is a `QTLEExperiment` object, `value` is a vector-like object with compatible dimensions to `object`.

`feature_id(object)`: Get the feature names.

`feature_id(object) <- value`: Set the feature names.

`variant_id(object)`: Get the variant names.

`variant_id(object) <- value`: Set the variant names.

## Author(s)

Christina B Azodi, Amelia Dunstone

## See Also

[QTLEExperiment](#), for the underlying class definition.

## Examples

```
qtle <- mockQTLE()
feature_id(qtle) <- gsub("gene", "Gene", feature_id(qtle))
feature_id(qtle)
variant_id(qtle) <- paste0(variant_id(qtle), "000")
variant_id(qtle)
```

---

qtle-state-id

---

*Modify and view state ID*


---

## Description

These are methods for getting or setting protected `colData` columns (i.e. `state_id`).

## Usage

```
## S4 method for signature 'QTLEExperiment'
state_id(object)

## S4 replacement method for signature 'QTLEExperiment'
state_id(object) <- value
```

**Arguments**

object is a [QTLEExperiment](#) object  
 value is a character vector with length equal to the number of columns/states in object.

**Details**

QTL are associations between a genetic variant and a quantitative state. The `state_id` methods can be used to get or set state IDs for all tests in a [QTLEExperiment](#) object. The values are stored in the `colData` as the `state_id` field so it can be easily accessed but not accidentally removed or overwritten.

**Value**

For `state_id`, a vector is returned containing the name of the state tested in each association. For `state_id<=`, a modified object is returned with the updated `state_ids` in `colData`, and in the `row.names` of the [QTLEExperiment](#) object.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```
qtle <- mockQTLE()
state_id(qtle) <- gsub("state", "State_", state_id(qtle))
state_id(qtle)
```

---

 QTLe-version

---

*Return the version of a [QTLEExperiment](#) object*


---

**Description**

Specifies the version of the [QTLEExperiment](#) package that an object of class [QTLEExperiment](#) was created with.

**Arguments**

object A [QTLEExperiment](#) object.

**Value**

A package version, of class [package\\_version](#).

**Available methods**

In the following code snippets, object is a [QTLEExperiment](#) objects.

`objectVersion(object)`: Return the version of the package with which object was constructed.

**Author(s)**

Christina B. Azodi, Amelia Dunstone

**See Also**

[QTLExperiment](#), for the underlying class definition and [updateObject](#) to update the object to the latest version.

**Examples**

```
qtle <- mockQTLE()
objectVersion(qtle)
```

---

QTLExperiment-class     *An S4 class to represent QTL summary statistics.*

---

**Description**

The QTLExperiment class is designed to represent multi-state QTL data. It inherits from the [RangedSummarizedExperiment](#) class. In addition, the class supports storage of multi-state adjusted beta and betaSE results (e.g., mash) and storage of summary results (e.g., pairwise sharing).

**Arguments**

|            |                                                                                                               |
|------------|---------------------------------------------------------------------------------------------------------------|
| ...        | Arguments passed to the <a href="#">SummarizedExperiment</a> constructor to fill the slots of the base class. |
| state_id   | An array of state IDs the length of ncol(qtle).                                                               |
| feature_id | An array of feature IDs the length of nrow(qtle).                                                             |
| variant_id | An array of variant IDs the length of nrow(qtle).                                                             |

**Details**

In this class, rows should represent associations (feature\_id:variant\_id pairs) while columns represent states (e.g. tissues). Assays include betas and error associated with the betas (e.g. standard errors). As with any [SummarizedExperiment](#) derivative, different information (e.g., test-statistics, significance calls) can be stored in user defined [assay](#) slots, and additional row and column meta-data can be attached using [rowData](#) and [colData](#), respectively.

The extra arguments in the constructor ([feature\\_id](#), [variant\\_id](#), and [state\\_id](#)) represent the main extensions implemented in the QTLExperiment class. This enables a consistent, formalized representation of key aspects of multi-state QTL data that are universal to the data structure. Readers are referred to the specific documentation pages for more details.

A QTLe can also be coerced from a [SummarizedExperiment](#) or [RangedSummarizedExperiment](#) instance.

**Value**

A QTLExperiment object.

**Slots**

`elementMetadata` A DataFrame containing at minimum `feature_id` and `variant_id` information. This is accessed using `rowData`.

`colData` A DataFrame containing at minimum `state_id` information.

`int_metadata` A list of additional metadata items to store.

**Author(s)**

Christina B Azodi

**Examples**

```
nStates <- 10
nQTL <- 100
betas <- matrix(rnorm(nStates * nQTL), ncol=nStates)
error <- matrix(abs(rnorm(nStates * nQTL)), ncol=nStates)

qtle <- QTLExperiment(
  assays=list(betas=betas, errors=error),
  feature_id=sample(1:10, nQTL, replace=TRUE),
  variant_id=sample(seq(1e3,1e5), nQTL),
  state_id=LETTERS[1:nStates])
qtle

## coercion from SummarizedExperiment
mock_sumstats <- mockSummaryStats(nStates=10, nQTL=100)
se <- SummarizedExperiment(
  assays=list(
    betas=mock_sumstats$betas,
    errors=mock_sumstats$errors))
as(se, "QTLExperiment")
```

---

subset

---

*Subsetting and replacing data in QTLExperiment objects*


---

**Description**

Includes methods to subset a [QTLExperiment](#) object by row and/or column and methods to replace all data for the specified rows and/or columns with another value. These methods ensure that all data fields remain synchronized when states or associations are removed. The [QTLExperiment](#) object is compatible with subsetting using square brackets or with the `subset` function.

**Usage**

```
## S4 method for signature 'QTLExperiment,ANY,ANY,ANY'
x[i, j, ..., drop = TRUE]

## S4 replacement method for signature 'QTLExperiment,ANY,ANY,QTLExperiment'
x[i, j, ...] <- value

## S4 method for signature 'QTLExperiment'
subset(x, i, ...)
```

**Arguments**

|       |                                                                                                               |
|-------|---------------------------------------------------------------------------------------------------------------|
| x     | is a <a href="#">QTLExperiment</a> object                                                                     |
| i     | is a vector of subscripts indicating the rows to retain.                                                      |
| j     | is a vector of subscripts indicating the columns to retain.                                                   |
| ...   | Further arguments to the subset function are passed to <code>S4Vectors:::evalqForSubset</code> .              |
| drop  | is passed to <code>SummarizedExperiment:::SummarizedExperiment-class</code> but is not used by those methods. |
| value | is the contents to be used for replacement.                                                                   |

**Value**

A [QTLExperiment](#) object.

**Subsetting**

In the following, x is a [QTLExperiment](#) object.

`x[i, j, ..., drop=TRUE]`: Returns a [QTLExperiment](#) containing the specified rows i and columns j, where i and j can be a logical, integer or character vector of subscripts, indicating the rows and columns, respectively, to retain. If either i or j is missing, than subsetting is only performed in the specified dimension. Arguments in ... and drop are passed to [\[, SummarizedExperiment-method\]](#).

**Replacing**

In the following, x is a [QTLExperiment](#) object.

`x[i, j, ...] <- value`: Replaces all data for rows i and columns j with the corresponding fields in a [QTLExperiment](#) value, where i and j can be a logical, integer, or character vector of subscripts, indicating the rows and columns, respectively, to retain. If either i or j is missing, than subsetting is only performed in the specified dimension. If both are missing, x is replaced entirely with value. Arguments in ... are passed to the corresponding [SummarizedExperiment](#) method.

**Author(s)**

Christina B Azodi

## Examples

```
qtile <- mockQTLE()

# Subsetting:
qtile[1:10,]
qtile[,1:5]

# Can also use subset()
qtile$WHEE <- sample(c("A", "B", "C"), ncol(qtile), replace=TRUE)
subset(qtile, , WHEE=="A")

# Can also use split()
split(qtile, sample(c("A", "B", "C"), nrow(qtile), replace=TRUE))
```

---

sumstats2qtile

*Coerce QTL summary statistics into a QTLExperiment object*


---

## Description

A suite of methods to extract QTL mapping summary statistics from common QTL workflow output files.

## Usage

```
sumstats2qtile(
  input,
  feature_id = "gene_id",
  variant_id = "variant_pos",
  betas = "slope",
  errors = "slope_se",
  pvalues = NULL,
  n_max = Inf,
  verbose = TRUE
)
```

## Arguments

|            |                                                                                                                                                                                                                                          |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| input      | Named array or data.frame with state name and the file to the QTL summary statistics for that state. If data.frame is provided, it must include columns 'state' and 'path'. Additional columns will be stored in the colData annotation. |
| feature_id | The name/index of the column with the feature_id info.                                                                                                                                                                                   |
| variant_id | The name/index of the column with the variant_id info.                                                                                                                                                                                   |
| betas      | The name/index of the column with the effect size/beta value.                                                                                                                                                                            |
| errors     | The name/index of the column with the effect size/beta standard error value.                                                                                                                                                             |
| pvalues    | The name/index of the column with the significance score.                                                                                                                                                                                |
| n_max      | Max number of rows to read per file. This is primarily used for testing purposes.                                                                                                                                                        |
| verbose    | logical. Whether to print progress messages.                                                                                                                                                                                             |

**Value**

A [QTLExperiment](#) object.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```
input_path <- system.file("extdata", package = "QTLExperiment")
state <- c("lung", "thyroid", "spleen", "blood")

# Input as a named array
input_list <- list(lung = paste0(input_path, "/GTEx_tx_lung.tsv"),
                  spleen = paste0(input_path, "/GTEx_tx_spleen.tsv"))

# Input as a data.frame.
# Must include columns 'state' and 'path'.
input_df <- data.frame(state = c("lung", "spleen"),
                      path = c(paste0(input_path, "/GTEx_tx_lung.tsv"),
                              paste0(input_path, "/GTEx_tx_spleen.tsv")))

# List version
qt1e1 <- sumstats2qt1e(input_list,
                      feature_id="molecular_trait_id",
                      variant_id="rsid",
                      betas="beta",
                      errors="se",
                      pvalues="pvalue",
                      verbose=TRUE)

qt1e1
head(betas(qt1e1))

# data.frame version
qt1e2 <- sumstats2qt1e(input_df,
                      feature_id="molecular_trait_id",
                      variant_id="rsid",
                      betas="beta",
                      errors="se",
                      pvalues="pvalue",
                      verbose=TRUE)

qt1e2
head(betas(qt1e2))
```

**Description**

Update [QTLEExperiment](#) objects to the latest version of the class structure. This is usually called by internal methods rather than by users or downstream packages.

**Usage**

```
## S4 method for signature 'QTLEExperiment'  
updateObject(object, ..., verbose = FALSE)
```

**Arguments**

|         |                                                                                         |
|---------|-----------------------------------------------------------------------------------------|
| object  | An old <a href="#">QTLEExperiment</a> object.                                           |
| ...     | Additional arguments that are ignored.                                                  |
| verbose | Logical scalar indicating whether a message should be emitted as the object is updated. |

**Details**

This function updates the [QTLEExperiment](#) to match changes in the internal class representation. Changes are as follows:

- No updates yet.

**Value**

An updated version of object.

**Author(s)**

Christina B Azodi

**See Also**

[objectVersion](#), which is used to determine if the object is up-to-date.

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