Package 'QTLExperiment'

November 12, 2026

Type Package

Date 2025-10-27

Title S4 classes for QTL summary statistics and metadata

Version 2.4.0

License GPL-3

URL https://github.com/dunstone-a/QTLExperiment

BugReports https://github.com/dunstone-a/QTLExperiment/issues

Encoding UTF-8

Depends SummarizedExperiment

Imports methods, rlang, checkmate, dplyr, collapse, vroom, tidyr, tibble, utils, stats, ashr, S4Vectors, BiocGenerics

Suggests testthat, BiocStyle, knitr, rmarkdown, covr

Description QLTExperiment 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.

biocViews FunctionalGenomics, DataImport, DataRepresentation, Infrastructure, Sequencing, SNP, Software

VignetteBuilder knitr

RoxygenNote 7.3.3

git_url https://git.bioconductor.org/packages/QTLExperiment

git_branch RELEASE_3_23

git_last_commit 67c5ec8

git_last_commit_date 2026-04-28

Repository Bioconductor 3.23

Date/Publication 2026-11-11

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`mockQTLE` *Mock data for the QTLExperiment object*

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
```

qtle-assays *Named assay getters and setters*

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))
```

QTLe-coerce *Coercing mash data objects into QTLe objects*

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 mash_set_data() or mash() from mashr.
sep	String separating the feature_id from the variant_id in the row.names of the mashr object
rowData	if feature_id and variant_id are not in the row.names, a rowData 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)
```

qtle-colData *Modify and view the colData of a QTLExperiment*

Description

Methods for changing the colData of a QTLExperiment.

Usage

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

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

Arguments

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

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 QTLExperiment object is returned with the updated colData.

Author(s)

Christina B Azodi, Amelia Dunstone

Examples

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

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

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

QTLe-combine *Combining QTLExperiment objects*

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

```
qtle <- mockQTLE()
qtle2 <- qtle
feature_id(qtle2) <- paste0("x", feature_id(qtle2))
rbind(qtle, qtle2)

qtle2 <- qtle
state_id(qtle2) <- paste0("x", state_id(qtle2))
cbind(qtle, qtle2)
```

QTLe-name *Return the name of a QTLExperiment object.*

Description

Returns the name of an object of class QTLExperiment.

Arguments

`object`	A QTLExperiment 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 QTLExperiment 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

QTLExperiment, for the underlying class definition.

Examples

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

QTLe-recover *Recover QTLExperiment IDs*

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 *rowData method for QTLExperiment*

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 QTLExperiment object is returned with the updated rowData.

Author(s)

Christina B Azodi, Amelia Dunstone

Examples

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

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

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

---

qtle-row_ids *Named rowData getters and setters*

Description

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

Arguments

object	is a QTLExperiment object.
value	is a vector with length equal to the number of rows of x.

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 QTLExperiment 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 QTLExperiment 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 QTLExperiment object.

Available methods

Here `object` is a QTLExperiment 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

QTLExperiment, 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 'QTLExperiment'
state_id(object)

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

Arguments

`object`	is a QTLExperiment 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 QTLExperiment 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 QTLExperiment 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 QTLExperiment object*

Description

Specifies the version of the QTLExperiment package that an object of class QTLExperiment was created with.

Arguments

`object`	A QTLExperiment object.

Value

A package version, of class package_version.

Available methods

In the following code snippets, `object` is a QTLExperiment 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 `SummarizedExperiment` 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 metadata 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 QTLExperiment 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 S4Vectors:::evalqForSubset.
drop	is passed to SummarizedExperiment:::SummarizedExperiment-class 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

```
qtle <- mockQTLE()

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

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

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

`sumstats2qtle` *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

```
sumstats2qtle(
  input,
  feature_id = "gene_id",
  variant_id = "variant_pos",
  betas = "slope",
  errors = "slope_se",
  pvalues = NULL,
  check_dupes = FALSE,
  gene_filter = NULL,
  col_types = NULL,
  delayed = FALSE,
  n_max = Inf,
  verbose = TRUE,
  otherFields = NULL
)
```

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.
check_dupes	logical. Whether to check for duplicate tests for some combinations of state, feature ID and variant ID. This is necessary for some data (e.g., xQTLatlas) where multiple genetic variants were tested for each feature and state. To avoid col_lists in the output object, this argument subsets to the first test for each combination. Note that checking that tests are unique can slow down run-times so should be avoided if not necessary.
gene_filter	A subset of the feature IDs to be retained in the object. Useful if you would like to load all variant ID tests for a particular feature, e.g., all tests in a particular region of a genome (e.g., for locus plots).
col_types	Column types e.g., a compact string "ccddd". For more information see vroom.
delayed	Logical scalar indicating whether matrices should be wrapped in DelayedArray. Not yet implemented.
n_max	Max number of rows to read per file. This is primarily used for testing purposes.
verbose	logical. Whether to print progress messages.
otherFields	The names of additional columns from the data that are to be passed into the QTLExperiment rowData. For example, this could include the positions of the variant IDs in terms of base pairs, or the name of the alternative allele.

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
qtle1 <- sumstats2qtle(input_list,
```

```
                        feature_id="molecular_trait_id",
                        variant_id="rsid",
                        betas="beta",
                        errors="se",
                        pvalues="pvalue",
                        verbose=TRUE)
qtle1
head(betas(qtle1))

# data.frame version
qtle2 <- sumstats2qtle(input_df,
                        feature_id="molecular_trait_id",
                        variant_id="rsid",
                        betas="beta",
                        errors="se",
                        pvalues="pvalue",
                        verbose=TRUE)
qtle2
head(betas(qtle2))
```

`updateObject` *Update a QTLExperiment object*

Description

Update QTLExperiment 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 'QTLExperiment'
updateObject(object, ..., verbose = FALSE)
```

Arguments

`object`	An old QTLExperiment 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 QTLExperiment 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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