

Package ‘QTLExperiment’

May 14, 2024

Type Package

Date 2023-09-28

Title S4 classes for QTL summary statistics and metadata

Version 1.3.0

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, ash, S4Vectors, BiocGenerics

Suggests testthat, BiocStyle, knitr, rmarkdown, covr

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.

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

VignetteBuilder knitr

RoxygenNote 7.3.1

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

git_branch devel

git_last_commit ea448bf

git_last_commit_date 2024-04-30

Repository Bioconductor 3.20

Date/Publication 2024-05-13

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mockQTLE	<i>Mock data for the QTLEExperiment object</i>
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Description

Functions to create fake input data for QTLEExperiments.

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 <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)
```

qtLe-col_ids

Named colData getters and setters

Description

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

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](#) and in the [int_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](#), [int_colData](#), and in the row.names of the [QTLExperiment](#) object.

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 [state_id](#) (for the getter) or [state_id<-](#) (for the setter).

state_id(x, ...), state_id(x, ...) <- value: Get or set the state (i.e. column) names.

Author(s)

Christina B Azodi

Examples

```
qtle <- mockQTLE()
state_id(qtle) <- sample(LETTERS, ncol(qtle), replace=TRUE)
state_id(qtle)
```

QTLe-combine

Combining QTLEExperiment objects

Description

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

Value

A [QTLEExperiment](#) object.

Combining

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

`rbind(..., deparse.level=1)`: Returns a [QTLEExperiment](#) 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 [QTLEExperiment](#) 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)
```

Description

Methods to get or set internal fields from the QTLExperiment class. These functions are intended for package developers who want to make changes or improvements to the object without breaking user code or to add protected fields to a QTLExperiment. They should *not* be used by general users.

Value

For assays, returns the value stored in the requested field of the internal rowData, colData or metaData.

For assays<-value, the relevant internal field of the QTLExperiment is updated.

Getters

Here x is a QTLExperiment.

int_rowData(x): Returns a [DataFrame](#) of internal row metadata, with number of rows equal to nrow(x) (analogous to the user-visible [rowData](#)).

int_colData(x): Returns a [DataFrame](#) of internal column metadata, with number of rows equal to ncol(x) (analogous to the user-visible [colData](#)).

int_metadata(x): Returns a list of internal metadata (analogous to the user-visible [metadata](#)).

The following methods can return visible and internal data in a single DataFrame.

rowData(x, ..., internal=TRUE): Returns a [DataFrame](#) of the user-visible row metadata with the internal row metadata added column-wise. A warning is emitted if the user-visible metadata column names overlap with the internal fields. Any arguments in ... are passed to [rowData, SummarizedExperiment-method](#).

colData(x, ..., internal=TRUE): Returns a [DataFrame](#) of the user-visible column metadata with the internal column metadata added column-wise. A warning is emitted if the user-visible metadata column names overlap with the internal fields. Any arguments in ... are passed to [colData, SummarizedExperiment-method](#).

Setters

Here x is a QTLExperiment.

int_rowData(x) <- value: Replaces the internal row metadata with value, a [DataFrame](#) with number of rows equal to nrow(x) (analogous to the user-visible [rowData<-](#)).

int_colData(x) <- value: Replaces the internal column metadata with value, a [DataFrame](#) with number of rows equal to ncol(x) (analogous to the user-visible [colData<-](#)).

int_metadata(x) <- value: Replaces the internal metadata with value (analogous to the user-visible [metadata<-](#)).

Comments

The internal metadata fields store additional elements that are parallel to the rows or columns of a [QTLEperiment](#) class. This avoids the need to specify new slots and adjust the subsetting/combining code for a new data element.

These elements being internal is important as it ensures that the implementation details are abstracted away. User interaction with these internal fields should be done via the designated getter and setter methods (e.g., [feature_id](#)), providing developers with freedom to change the internal representation without breaking user code.

Author(s)

Christina B Azodi

See Also

[colData](#), [rowData](#) and [metadata](#) for the user-visible equivalents.

Examples

```
qtle <- mockQTLE()
int_metadata(qtle)$whee <- 1
```

QTLe-name	<i>Return the name of a QTLEperiment object.</i>
-----------	--

Description

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

Arguments

x	A QTLEperiment object.
value	Any character-like object or NULL to remove existing labels.

Value

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

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

Available methods

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

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

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

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

Author(s)

Christina B. Azodi

See Also

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

Examples

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

QTLe-recover

Recover QTLEExperiment 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 QTLEExperiment object

Value

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

Examples

```
# Recover a column in colData

qtle <- mockQTLE()

head(colData(qtle))

new_colData <- DataFrame(
  list(some_info1=LETTERS[1:ncol(qtle)],
       some_info2=c(1:ncol(qtle))))

# colData is overwritten
colData(qtle) <- new_colData
```

```

head(colData(qtle))

# colData is recovered
qtle <- recover_qtle_ids(qtle)
head(colData(qtle))

# Recover information from rowData

head(rowData(qtle))

# variant_id are shuffled accidentally
rowData(qtle)$variant_id <- sample(rowData(qtle)$variant_id, nrow(qtle))
head(rowData(qtle))

# Recover rowData
qtle <- recover_qtle_ids(qtle)
head(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).

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](#) and in the [int_rowData](#) compartments so they can be easily accessed but not accidentally removed or overwritten.

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](#), [int_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](#), [int_rowData](#), and in the row.names of the [QTLExperiment](#) object.

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 [feature_id](#) (for the getter) or [feature_id<-](#) (for the setter).

[feature_id\(x, ...\)](#), [feature_id\(x, ...\) <- value](#): Get or set the feature (e.g. gene, metabolite) names.

[variant_id\(x, ...\)](#), [variant_id\(x, ...\) <- value](#): Get or set the variant (i.e. SNP) names.

Author(s)

Christina B Azodi

See Also

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

Examples

```
qtle <- mockQTLE()
feature_id(qtle) <- sample(LETTERS, nrow(qtle), replace=TRUE)
feature_id(qtle)
variant_id(qtle) <- sample(paste0("rsid", 1:100), nrow(qtle), replace=TRUE)
variant_id(qtle)
```

QTLe-subset

Subsetting and replacing data in QTLEExperiment objects

Description

Includes methods to subset a [QTLEExperiment](#) 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.

Value

A [QTLEExperiment](#) object.

Subsetting

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

`x[i, j, ..., drop=TRUE]`: Returns a [QTLEExperiment](#) 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 [QTLEExperiment](#) object.

`x[i, j, ...] <- value`: Replaces all data for rows *i* and columns *j* with the corresponding fields in a [QTLEExperiment](#) 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))
```

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

x A [QTLEExperiment](#) object.

Value

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

Available methods

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

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

Author(s)

Christina B. Azodi, Amelia Dunstone

See Also

[QTLEExperiment](#), 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. that are commonly encountered during single-cell data analysis. 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

int_rowData	A DataFrame containing at minimum feature_id and variant_id information
int_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")

```

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,
  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 `QTLEExperiment` object.

Author(s)

Christina B Azodi, Amelia Dunstone

Examples

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

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

# List version
qt1e1 <- sumstats2qtle(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 <- sumstats2qtle(input_df,
                      feature_id="molecular_trait_id",
                      variant_id="rsid",
                      betas="beta",
                      errors="se",
                      pvalues="pvalue",
                      verbose=TRUE)
```

```
qt1e2  
head(betas(qt1e2))
```

updateObject	<i>Update a QTLEExperiment object</i>
--------------	---------------------------------------

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 QTLEExperiment 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.

Examples

```
qt1e <- mockQTLE()
objectVersion(qt1e)

qt1e_new <- QTLEExperiment::updateObject(qt1e)
```

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