Package ‘QTLExperiment’

January 12, 2024

Type Package
Date 2023-09-28
Title S4 classes for QTL summary statistics and metadata
Version 1.0.0
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 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 7.2.3
git_url https://git.bioconductor.org/packages/QTLExperiment
git_branch RELEASE_3_18
git_last_commit eb387bf
git_last_commit_date 2023-10-24
Repository Bioconductor 3.18
Date/Publication 2024-01-11
**mockQTLE**

**Author** Christina Del Azodi [aut],
Davis McCarthy [ctb],
Amelia Dunstone [cre, ctb] (<https://orcid.org/0009-0009-6426-1529>)

**Maintainer** Amelia Dunstone <amelia.dunstone@svi.edu.au>

**R topics documented:**

- mockQTLE .................................................. 2
- qtle-assays ................................................. 3
- QTLExperiment ............................................. 4
- qtle-col_ids ................................................ 5
- QTLExperiment-class ..................................... 6
- QTLExperiment-class ..................................... 7
- QTLExperiment ............................................ 8
- QTLExperiment ............................................ 9
- qtle-row_ids .............................................. 10
- QTLExperiment ............................................ 11
- QTLExperiment ............................................ 12
- QTLExperiment ............................................ 13
- sumstats2qtle ............................................. 14
- updateObject ............................................. 16

**Index**

mockQTLE  Mock data for the QTLExperiment object

---

**Description**

Functions to create fake input data for QTLExperiments.

**Usage**

```r
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
```r
nStates <- 6
nQTL <- 40

# Mock QTLEperiment data
tle <- mockQTLE(nStates, nQTL)
dim(tle)

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 \(\text{assay}(\text{qtle}, \text{i}=\text{X}, \ldots)\) where \text{qtle} is a \text{QTLEperiment} object and \text{X} is the name of the method. For example, \text{betas} will get or set \(\text{X}=	ext{"betas"}\).

Value
For \text{assays}, returns the value stored in the requested \text{assay}.
For \text{assays<}-value, the relevant slot of the \text{QTLEperiment} is updated.

Available methods
Here \text{x} is a \text{QTLEperiment} object, \text{value} is a matrix-like object with the same dimensions as \text{x}, and \ldots are further arguments passed to \text{assay} (for the getter) or \text{assay<} (for the setter).

```
betas(x, \ldots), betas(x, \ldots)<- 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))

---

**QTL-coerce**

Coercing mash data objects into QTL objects

Description

Function to coerce a mashr object (class list or mashr) into a QTL 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.
**qtle-col_ids**

**Value**

A `QTLExperiment` object.

**Author(s)**

Christina B Azodi, Amelia Dunstone

**Examples**

```r
nStates <- 6
nQTL <- 40
mashr_sim <- mockMASHR(nStates, nQTL)
qtle2 <- mash2qtle(
  mashr_sim,
  rowData=DataFrame(feature_id=row.names(mashr_sim$Bhat),
                  variant_id=sample(seq_len(nQTL))),
  rowData=DataFrame(feature_id=row.names(mashr_sim$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

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

### 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

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

```r
qtle2 <- qtle
state_id(qtle2) <- paste0("x", state_id(qtle2))
cbind(qtle, qtle2)
```
Internal QTLExperiment functions

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 QTLExperiment 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

---

\textbf{QTLe-name}

\textit{Return the name of a QTLExperiment object.}

Description

Returns the name of an object of class QTLExperiment.

Arguments

\begin{itemize}
  \item \textbf{x} A QTLExperiment object.
  \item \textbf{value} Any character-like object or \texttt{NULL} to remove existing labels.
\end{itemize}

Value

For mainExpName(x), returns the name associated to \textit{x}.
For mainExpName(x) <- value, the name of the object \textit{x} is updated.

Available methods

In the following code snippets, \textit{x} is a QTLExperiment objects.

mainExpName(x): Return the name assigned to \textit{x}.
mainExpName(x) <- value: Change the name assigned to \textit{x} to \textit{value}.
mainExpName(x) <- \texttt{NULL}: Remove the name associated to \textit{x}.
QTLrecovery

Author(s)
Christina B. Azodi

See Also
QTLExperiment, for the underlying class definition.

Examples
qtle <- mockQTLEx()
mainExpName(qtle)
mainExpName(qtle) <- "test_name"
mainExpName(qtle)

---

QTLrecovery  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.

Examples
# Recover a column in colData
qtle <- mockQTLEx()
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

QTLExperiment, 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 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.

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.
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))

---

Description

Return the version of a QTLExperiment object

Arguments

x A QTLExperiment object.

Value

A package version, of class package_version.

Available methods

In the following code snippets, x is a QTLExperiment objects.

objectVersion(x): Return the version of the package with which x 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

```r
qtle <- mockQTLEx()
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
**Examples**

```r
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")
```

---

**Description**

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

**Usage**

```r
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 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)
updateObject(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.
Examples

```r
qtle <- mockQTL()
objectVersion(qtle)

qtle_new <- QTL::QTL::QTLExperiment::updateObject(qtle)
```
Index

.mashData_2_qtle (QTLe-coerce), 4
.mashFit_2_qtle (QTLe-coerce), 4
[,QTLEperiment,ANY,ANY,ANY-method (QTLe-subset), 11
[,QTLEperiment,ANY,ANY-method (QTLe-subset), 11
[,QTLEperiment,ANY-method (QTLe-subset), 11
[<-,QTLEperiment,ANY,ANY,QTLEperiment-method (QTLe-subset), 11

assay, 3, 4, 13

betas (qtle-assays), 3
betas,QTLEperiment-method (qtle-assays), 3
betas<- (qtle-assays), 3
betas<-,QTLEperiment-method (qtle-assays), 3

cbind, 6
cbind,QTLEperiment-method (QTLe-combine), 6

coerce,RangedSummarizedExperiment,QTLEperiment-method (QTLe-class), 13
coerce,SummarizedExperiment,QTLEperiment-method (QTLe-class), 13

colData, 5, 7, 8, 13
colData,QTLEperiment-method (QTLe-internals), 7

Dataframe, 7

errors (qtle-assays), 3
errors,QTLEperiment-method (qtle-assays), 3
errors<- (qtle-assays), 3
errors<-,QTLEperiment-method (qtle-assays), 3

feature_id, 8, 10, 13

int_colData, 5
int_colData (QTLe-internals), 7

int_rowData, 10
int_rowData (QTLe-internals), 7

lfsrs (qtle-assays), 3
lfsrs,QTLEperiment-method (qtle-assays), 3
lfsrs<- (qtle-assays), 3
lfsrs<-,QTLEperiment-method (qtle-assays), 3

mainExpName (QTLe-name), 8
mainExpName,QTLEperiment-method (QTLe-name), 8
mainExpName<- (QTLe-name), 8
mainExpName<-,QTLExperiment,character OR NULL-method (QTLName), 8
mash2qtle (QTL-coerce), 4
metadata, 7, 8
mockMASHR (mockQTL), 2
mockMASHR_FIT (mockQTL), 2
mockQTL, 2
mockSummaryStats (mockQTL), 2

objectVersion, 16
objectVersion (QTL-version), 12
objectVersion, QTLExperiment-method (QTL-version), 12

package_version, 12
parallel_slot_names, QTLExperiment-method (QTL-internals), 7
pvalues (qtl-assays), 3
pvalues, QTLExperiment-method (qtl-assays), 3
pvalues<-, (qtl-assays), 3
pvalues<-, QTLExperiment-method (qtl-assays), 3

qtl-assays, 3
QTL-coerce, 4
qtl-col_ids, 5
QTL-combine, 6
QTL-internals, 7
QTL-name, 8
QTL-recover, 9
qtl-row_ids, 10
QTL-subset, 11
QTL-version, 12
QTLExperiment, 3, 5–12, 15, 16
QTLExperiment (QTLExperiment-class), 13
QTLExperiment-class, 13

RangedSummarizedExperiment, 13
rbind, 6
rbind, QTLExperiment-method (QTL-combine), 6
recover_qtl_ids (QTL-recover), 9
rowData, 7, 8, 10, 13
rowData, QTLExperiment-method (QTL-internals), 7

state_id, 5, 13
state_id (qtl-col_ids), 5