

Package ‘MultiAssayExperiment’

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Title Software for the integration of multi-omics experiments in
Bioconductor

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Description Harmonize data management of multiple experimental assays performed on an overlapping set of specimens. It provides a familiar Bioconductor user experience by extending concepts from SummarizedExperiment, supporting an open-ended mix of standard data classes for individual assays, and allowing subsetting by genomic ranges or rownames. Facilities are provided for reshaping data into wide and long formats for adaptability to graphing and downstream analysis.

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URL <http://waldronlab.io/MultiAssayExperiment/>

BugReports <https://github.com/waldronlab/MultiAssayExperiment/issues>

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'MultiAssayExperiment-subset.R'
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'MultiAssayExperimentToMAFR' 'assay-methods.R' 'data.R'
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MultiAssayExperiment-package

MultiAssayExperiment: Build an integrative multi-assay container

Description

MultiAssayExperiment allows the manipulation of related multiassay datasets with partially overlapping samples, associated metadata at the level of an entire study, and at the level of the "biological unit". The biological unit may be a patient, plant, yeast strain, etc.

Details

The package hierarchy of information:

- study
- experiments
- samples

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See Also

Useful links:

- <http://waldronlab.io/MultiAssayExperiment/>
- Report bugs at <https://github.com/waldronlab/MultiAssayExperiment/issues>

ExperimentList	<i>Represent multiple experiments as a List-derivative ExperimentList</i>
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Description

The ExperimentList class can contain several different types of data. The only requirements for an ExperimentList class are that the objects contained have the following set of methods: dim, [, dimnames

Usage

```
ExperimentList(...)
```

Arguments

... A named list class object

Value

A ExperimentList class object of experiment data

Examples

```
## Create an empty ExperimentList instance
ExperimentList()

## Create array matrix and AnnotatedDataFrame to create an ExpressionSet class
arraydat <- matrix(data = seq(101, length.out = 20), ncol = 4,
  dimnames = list(
    c("ENST00000294241", "ENST00000355076",
      "ENST00000383706", "ENST00000234812", "ENST00000383323"),
    c("array1", "array2", "array3", "array4")
  ))

colDat <- data.frame(slope53 = rnorm(4),
  row.names = c("array1", "array2", "array3", "array4"))

## SummarizedExperiment constructor
exprdat <- SummarizedExperiment::SummarizedExperiment(arraydat,
  colData = colDat)

## Create a sample methylation dataset
methyldat <- matrix(data = seq(1, length.out = 25), ncol = 5,
  dimnames = list(
    c("ENST00000355076", "ENST00000383706",
      "ENST00000383323", "ENST00000234812", "ENST00000294241"),
    c("methy11", "methy12", "methy13",
      "methy14", "methy15")
  ))
```

```

## Create a sample RNASeqGene dataset
rnadat <- matrix(
  data = sample(c(46851, 5, 19, 13, 2197, 507,
    84318, 126, 17, 21, 23979, 614), size = 20, replace = TRUE),
  ncol = 4,
  dimnames = list(
    c("XIST", "RPS4Y1", "KDM5D", "ENST00000383323", "ENST00000234812"),
    c("smparray1", "smparray2", "smparray3", "smparray4")
  ))

## Create a mock RangedSummarizedExperiment from a data.frame
rangedat <- data.frame(chr="chr2", start = 11:15, end = 12:16,
  strand = c("+", "-", "+", "*", "."),
  samp0 = c(0,0,1,1,1), samp1 = c(1,0,1,0,1), samp2 = c(0,1,0,1,0),
  row.names = c(paste0("ENST", "00000", 135411:135414), "ENST00000383323"))

rangeSE <- SummarizedExperiment::makeSummarizedExperimentFromDataFrame(rangedat)

## Combine to a named list and call the ExperimentList constructor function
assayList <- list(Affy = exprdat, Methyl450k = methylat, RNASeqGene = rnadat,
  GISTIC = rangeSE)

## Use the ExperimentList constructor
ExpList <- ExperimentList(assayList)

```

ExperimentList-class *ExperimentList - A container for multi-experiment data*

Description

The ExperimentList class is a container that builds on the SimpleList with additional checks for consistency in experiment names and length. It contains a SimpleList of experiments with sample identifiers. One element present per experiment performed.

Convert from SimpleList or list to the multi-experiment data container. When using the **mergeReplicates** method, additional arguments are passed to the given simplify function argument (e.g., na.rm = TRUE)

Usage

```

## S4 method for signature 'ExperimentList'
show(object)

## S4 method for signature 'ExperimentList'
isEmpty(x)

## S4 method for signature 'ExperimentList'
dimnames(x)

## S4 method for signature 'ExperimentList'

```

```

colnames(x, do.NULL = TRUE, prefix = "col")

## S4 method for signature 'ExperimentList'
rownames(x, do.NULL = TRUE, prefix = "row")

## S4 method for signature 'ExperimentList'
mergeReplicates(x, replicates = list(), simplify = BiocGenerics::mean, ...)

## S4 method for signature 'ANY,missing'
assay(x, i, withDimnames = TRUE, ...)

## S4 method for signature 'ExperimentList'
assays(x, withDimnames = TRUE, ...)

## S4 method for signature 'ExperimentList,missing'
assay(x, i, withDimnames = TRUE, ...)

## S4 method for signature 'ExperimentList,numeric'
assay(x, i, withDimnames = TRUE, ...)

## S4 method for signature 'ExperimentList,character'
assay(x, i, withDimnames = TRUE, ...)

```

Arguments

object, x	An ExperimentList object
do.NULL, prefix	See <code>?base::rownames</code> for a description of these arguments.
replicates	<code>mergeReplicates</code> : A list or LogicalList where each element represents a sample and a vector of repeated measurements for the sample
simplify	A function for merging columns where duplicates are indicated by replicates
...	Additional arguments. See details for more information.
i	A scalar character or integer index
withDimnames	logical (default TRUE) whether to return dimension names

Value

An `ExperimentList` class object

Methods (by generic)

- `show(ExperimentList)`: Show method for [ExperimentList](#) class
- `isEmpty(ExperimentList)`: check for zero length across all experiments
- `dimnames(ExperimentList)`: Get the dimension names for an `ExperimentList` using [CharacterList](#)
- `colnames(ExperimentList)`: Get the column names for an `ExperimentList` as a [CharacterList](#) slightly more efficiently
- `rownames(ExperimentList)`: Get the row names for an `ExperimentList` as a [CharacterList](#) slightly more efficiently

- `mergeReplicates(ExperimentList)`: Apply the `mergeReplicates` method on the `ExperimentList` elements
- `assay(x = ANY, i = missing)`: Obtain the specified assay with a numeric or character reference
- `assays(ExperimentList)`: Get the assay data from each element in the [ExperimentList](#)

coercion

Convert a list or S4 List to an `ExperimentList` using the `as()` function.

In the following example, `x` is either a list or [List](#):

```
as(x, "ExperimentList")
```

Examples

```
ExperimentList()
```

hasAssay

Checking assay method for any class

Description

The `hasAssay` function is intended for developers who would like to include new classes into a `MultiAssayExperiment` instance. It checks the methods tables of the assay function for the specified class of the argument.

Usage

```
hasAssay(object)
```

Arguments

`object` A `MultiAssayExperiment` or named list object instance

Value

A logical value indicating method availability

Examples

```
lst <- structure(list(), .Names=character())
hasAssay(lst)
```

HDF5MultiAssayExperiment

Save a MultiAssayExperiment class object to HDF5 and Rds files

Description

This function takes a `MultiAssayExperiment` object and uses the assays functionality to obtain data matrices out of the experiments. These are then saved into the `.h5` file format. This function relies heavily on the `HDF5Array` package whose installation is required before use. `saveHDF5MultiAssayExperiment` preserves the classes contained in the `ExperimentList` with the exception of `matrix` which is converted to `HDF5Matrix`. Internal `SummarizedExperiment` assays are converted to HDF5-backed assays as in `HDF5Array::saveHDF5SummarizedExperiment`. `SummarizedExperiment` objects with multiple `i`-th assays will have the first assay take precedence and others assays will be dropped with a warning. If the first assay in a `SummarizedExperiment` contains an array, the array is preserved in the process of saving and loading the HDF5-backed `MultiAssayExperiment`.

Usage

```
saveHDF5MultiAssayExperiment(
  x,
  dir = "h5_mae",
  prefix = NULL,
  replace = FALSE,
  chunkdim = NULL,
  level = NULL,
  as.sparse = NA,
  verbose = NA
)

loadHDF5MultiAssayExperiment(dir = "h5_mae", prefix = NULL)
```

Arguments

<code>x</code>	A <code>MultiAssayExperiment</code> object or derivative
<code>dir</code>	The path (as a single string) to the directory where to save the HDF5-based <code>MultiAssayExperiment</code> object or to load it from. When saving, the directory will be created if it doesn't already exist. If the directory already exists and no prefix is specified and <code>replace</code> is set to <code>TRUE</code> , then it's replaced with an empty directory.
<code>prefix</code>	An optional prefix to add to the names of the files created inside <code>dir</code> . This allows saving more than one object in the same directory. When the prefix is <code>NULL</code> , the name of the <code>x</code> input <code>MultiAssayExperiment</code> is used. To avoid the default setting use an empty character string i.e., <code>""</code> . An underscore (<code>_</code>) is appended to the prefix when provided; therefore, typical inputs should be words, e.g., <code>"test"</code> .
<code>replace</code>	When no prefix is specified, should a pre-existing directory be replaced with a new empty one? The content of the pre-existing directory will be lost!

chunkdim, level	The dimensions of the chunks and the compression level to use for writing the assay data to disk. Passed to the internal calls to <code>wri teHDF5Array</code> . See ?writeHDF5Array for more information.
as.sparse	Whether the assay data should be flagged as sparse or not. If set to NA (the default), then the specific <code>as.sparse</code> value to use for each assay is determined by calling <code>is_sparse()</code> on them. Passed to the internal calls to <code>wri teHDF5Array</code> . See ?writeHDF5Array for more information and an IMPORTANT NOTE.
verbose	Set to TRUE to make the function display progress. In the case of <code>saveHDF5MultiAssayExperiment()</code> , <code>verbose</code> is set to NA by default, in which case verbosity is controlled by <code>DelayedArray.verbose.block.processing</code> option. Setting <code>verbose</code> to TRUE or FALSE overrides the option.

Value

- `saveHDF5MultiAssayExperiment`: saves an Rds and h5 file to a directory from the input `MultiAssayExperiment`
- `loadHDF5MultiAssayExperiment`: a `MultiAssayExperiment` object loaded from a folder as saved by `saveHDF5MultiAssayExperiment`

Examples

```
data("miniACC")

testDir <- file.path(tempdir(), "test_mae")

saveHDF5MultiAssayExperiment(
  miniACC, dir = testDir, verbose = TRUE, replace = TRUE
)

## inspect the files in the dir
list.files(testDir)

loadHDF5MultiAssayExperiment(
  dir = testDir
)

## remove example files
unlink(testDir, recursive = TRUE)
```

listToMap

Convert map from data.frame or DataFrame to list and vice versa

Description

The `mapToList` function provides a convenient way of reordering a `data.frame` to a list. The `listToMap` function does the opposite by taking a list and converting it to `DataFrame`.

Usage

```
listToMap(listmap, fill = TRUE)

mapToList(dfmap, assayCol = "assay")
```

Arguments

listmap	A named list object containing DataFrames with "primary" and "colname" columns
fill	logical(1) Whether to fill the map with an empty DataFrame when empty elements are present in the input list
dfmap	A data.frame or DataFrame object with identifiers in the first column
assayCol	A character vector of length one indicating the assay names column

Value

A [DataFrame](#) class object of names
 A list object of DataFrames for each assay

Functions

- listToMap(): The inverse of the listToMap operation

Examples

```
example("MultiAssayExperiment")

## Create a sampleMap from a list using the listToMap function
sampMap <- listToMap(maplist)

## The inverse operation is also available
maplist <- mapToList(sampMap)
```

MatchedAssayExperiment-class

MatchedAssayExperiment - A matched-samples MultiAssayExperiment class

Description

This class supports the use of matched samples where an equal number of observations per biological unit are present in all assays.

Usage

```
MatchedAssayExperiment(...)
```

Arguments

... Either a single `MultiAssayExperiment` or the components to create a valid `MultiAssayExperiment`

Value

A `MatchedAssayExperiment` object

Functions

- `MatchedAssayExperiment()`: Construct a `MatchedAssayExperiment` class from [MultiAssayExperiment](#)

See Also

[MultiAssayExperiment](#)

Examples

```
data("miniACC")
acc <- as(miniACC, "MatchedAssayExperiment")
acc
```

miniACC

Adrenocortical Carcinoma (ACC) MultiAssayExperiment

Description

A [MultiAssayExperiment](#) object providing a reduced version of the TCGA ACC dataset for all 92 patients. RNA-seq, copy number, and somatic mutations are included only for genes whose proteins are included in the reverse-phase protein array. The MicroRNA-seq dataset is also included, with infrequently expressed microRNA removed. Clinical, pathological, and subtype information are provided by `colData(miniACC)`, and some additional details are provided by `metadata(miniACC)`.

Usage

```
data("miniACC")
```

Format

A `MultiAssayExperiment` with 5 experiments, providing:

RNASeq2GeneNorm RNA-seq count data: an `ExpressionSet` with 198 rows and 79 columns

gistic2 Recurrent copy number lesions identified by GISTIC2: a `SummarizedExperiment` with 198 rows and 90 columns

RPPAArray Reverse Phase Protein Array: an `ExpressionSet` with 33 rows and 46 columns.

Rows are indexed by genes, but protein annotations are available from `featureData(miniACC[["RPPAArray"]])`.

The source of these annotations is noted in `abstract(miniACC[["RPPAArray"]])`

Mutations Somatic mutations: a matrix with 223 rows and 90 columns. 1 for any kind of non-silent mutation, zero for silent (synonymous) or no mutation.

miRNASeqGene microRNA sequencing: an ExpressionSet with 471 rows and 80 columns. Rows not having at least 5 counts in at least 5 samples were removed.

Author(s)

Levi Waldron <lwaldron.research@gmail.com>

Source

<https://github.com/waldronlab/multiassayexperiment-tcga>

References

Zheng S *et al.*: Comprehensive Pan-Genomic Characterization of Adrenocortical Carcinoma. Cancer Cell 2016, 29:723-736.

Examples

```
data("miniACC")
metadata(miniACC)
colnames(colData(miniACC))
table(miniACC$vital_status)
longFormat(
  miniACC["MAPK3", , ],
  colDataCols = c("vital_status", "days_to_death")
)

wideFormat(
  miniACC["MAPK3", , ],
  colDataCols = c("vital_status", "days_to_death")
)
```

MultiAssayExperiment *Construct an integrative representation of multi-omic data with MultiAssayExperiment*

Description

The constructor function for the [MultiAssayExperiment](#) combines multiple data elements from the different hierarchies of data (study, experiments, and samples). It can create instances where neither a sampleMap or a colData set is provided. Please see the MultiAssayExperiment API documentation for more information.

Usage

```
MultiAssayExperiment(
  experiments = ExperimentList(),
  colData = S4Vectors::DataFrame(),
  sampleMap = S4Vectors::DataFrame(assay = factor(), primary = character(), colname =
    character()),
  metadata = list(),
  drops = list()
)
```

Arguments

experiments	A list or ExperimentList of all combined experiments
colData	A DataFrame or <code>data.frame</code> of characteristics for all biological units
sampleMap	A DataFrame or <code>data.frame</code> of assay names, sample identifiers, and colname samples
metadata	An optional argument of "ANY" class (usually list) for content describing the experiments
drops	A list of unmatched information (included after subsetting)

Value

A `MultiAssayExperiment` object that can store experiment and phenotype data

colData

The `colData` input can be either `DataFrame` or `data.frame` with subsequent coercion to `DataFrame`. The rownames in the `colData` must match the colnames in the `experiments` if no `sampleMap` is provided.

experiments

The `experiments` input can be of class [SimpleList](#) or `list`. This input becomes the [ExperimentList](#). Each element of the input `list` or `List` must be named, rectangular with two dimensions, and have `dimnames`.

sampleMap

The `sampleMap` can either be input as `DataFrame` or `data.frame` with eventual coercion to `DataFrame`. The `sampleMap` relates biological units and biological measurements within each assay. Each row in the `sampleMap` is a single such link. The standard column names of the `sampleMap` are "assay", "primary", and "colname". Note that the "assay" column is a factor corresponding to the names of each experiment in the `ExperimentList`. In the case where these names do not match between the `sampleMap` and the `experiments`, the documented experiments in the `sampleMap` take precedence and experiments are dropped by the harmonization procedure. The constructor function will generate a `sampleMap` in the case where it is not provided and this method may be a 'safer' alternative for creating the `MultiAssayExperiment` (so long as the rownames are identical in the `colData`, if provided). An empty `sampleMap` may produce empty experiments if the levels of the "assay" factor in the `sampleMap` do not match the names in the `ExperimentList`.

See Also

[MultiAssayExperiment](#)

Examples

```
## Run the example ExperimentList
example("ExperimentList")

## Create sample maps for each experiment
exprmap <- data.frame(
  primary = c("Jack", "Jill", "Barbara", "Bob"),
  colname = c("array1", "array2", "array3", "array4"),
  stringsAsFactors = FALSE)

methylmap <- data.frame(
  primary = c("Jack", "Jack", "Jill", "Barbara", "Bob"),
  colname = c("methyl1", "methyl2", "methyl3", "methyl4", "methyl5"),
  stringsAsFactors = FALSE)

rnamap <- data.frame(
  primary = c("Jack", "Jill", "Bob", "Barbara"),
  colname = c("samparray1", "samparray2", "samparray3", "samparray4"),
  stringsAsFactors = FALSE)

gistmap <- data.frame(
  primary = c("Jack", "Bob", "Jill"),
  colname = c("samp0", "samp1", "samp2"),
  stringsAsFactors = FALSE)

## Combine as a named list and convert to a DataFrame
maplist <- list(Affy = exprmap, Methyl450k = methylmap,
  RNASeqGene = rnamap, GISTIC = gistmap)

## Create a sampleMap
sampMap <- listToMap(maplist)
## Create an example phenotype data
colDat <- data.frame(sex = c("M", "F", "M", "F"), age = 38:41,
  row.names = c("Jack", "Jill", "Bob", "Barbara"))

## Create a MultiAssayExperiment instance
mae <- MultiAssayExperiment(experiments = ExpList, colData = colDat,
  sampleMap = sampMap)
```

MultiAssayExperiment-class

MultiAssayExperiment - An integrative multi-assay class for experiment data

Description

The MultiAssayExperiment class can be used to manage results of diverse assays on a collection of specimen. Currently, the class can handle assays that are organized instances of [SummarizedExperiment](#), [ExpressionSet](#), matrix, [RaggedExperiment](#) (inherits from [GRangesList](#)), and [RangedVcfStack](#). Create new MultiAssayExperiment instances with the homonymous constructor, minimally with the argument [ExperimentList](#), potentially also with the arguments colData (see section below) and [sampleMap](#).

Usage

```
## S4 method for signature 'MultiAssayExperiment'
show(object)

## S4 method for signature 'MultiAssayExperiment'
length(x)

## S4 method for signature 'MultiAssayExperiment'
names(x)

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

## S4 method for signature 'MultiAssayExperiment'
dimnames(x)

## S4 method for signature 'MultiAssayExperiment'
c(x, ..., sampleMap = NULL, mapFrom = NULL)

## S4 method for signature 'MultiAssayExperiment'
exportClass(
  object,
  dir = tempdir(),
  fmt,
  ext,
  match = FALSE,
  verbose = TRUE,
  ...
)

## S4 method for signature 'MultiAssayExperiment'
assays(x, withDimnames = TRUE, ...)

## S4 method for signature 'MultiAssayExperiment,missing'
assay(x, i, withDimnames = TRUE, ...)

## S4 method for signature 'MultiAssayExperiment,numeric'
assay(x, i, withDimnames = TRUE, ...)
```

```
## S4 method for signature 'MultiAssayExperiment,character'
assay(x, i, withDimnames = TRUE, ...)
```

Arguments

object, x	A MultiAssayExperiment object
...	Additional arguments for supporting functions. See details.
verbose	logical(1) Whether to print additional information (default TRUE)
sampleMap	c method: a sampleMap list or DataFrame to guide merge
mapFrom	Either a logical, character, or integer vector indicating the experiment(s) that have an identical colname order as the experiment input(s). If using a character input, the name must match exactly.
dir	character(1) A directory for saving exported data (default: tempdir())
fmt	character(1) or function() Either a format character atomic as supported by write.table either ('csv', or 'tsv') or a function whose first two arguments are 'object to save' and 'file location'
ext	character(1) A file extension supported by the format argument
match	logical(1) Whether to coerce the current object to a 'MatchedAssayExperiment' object (default: FALSE)
withDimnames	logical (default TRUE) whether to return dimension names included in the object
i	An integer or character scalar indicating the assay to return

Details

The dots (...) argument allows the user to specify additional arguments in several instances.

- subsetting [: additional arguments sent to [findOverlaps](#).
- mergeReplicates: used to specify arguments for the simplify functional argument
- assay: may contain withDimnames, which is forwarded to assays
- combining c: compatible MultiAssayExperiment classes passed on to the [ExperimentList](#) constructor, can be a list, [List](#), or a series of named arguments. See the examples below.

Value

A MultiAssayExperiment object

Methods (by generic)

- show(MultiAssayExperiment): Show method for a MultiAssayExperiment
- length(MultiAssayExperiment): Get the length of ExperimentList
- names(MultiAssayExperiment): Get the names of the ExperimentList
- updateObject(MultiAssayExperiment): Update old serialized MultiAssayExperiment objects to new API

- `dimnames(MultiAssayExperiment)`: Get the dimension names for a `MultiAssayExperiment` object
- `c(MultiAssayExperiment)`: Add a supported data class to the `ExperimentList`
- `exportClass(MultiAssayExperiment)`: Export data from class to a series of text files
- `assays(MultiAssayExperiment)`: Obtain a `SimpleList` of assay data for all available experiments in the object
- `assay(x = MultiAssayExperiment, i = missing)`: Convenience function for extracting the assay of the first element (default) in the `ExperimentList`. A numeric or character index can also be provided

Slots

`ExperimentList` A `ExperimentList` class object for each assay dataset

`colData` A `DataFrame` of all clinical/specimen data available across experiments

`sampleMap` A `DataFrame` of translatable identifiers of samples and participants

`metadata` Additional data describing the `MultiAssayExperiment` object

`drops` A metadata list of dropped information

colData

The `colData` slot is a collection of primary specimen data valid across all experiments. This slot is strictly of class `DataFrame` but arguments for the constructor function allow arguments to be of class `data.frame` and subsequently coerced.

ExperimentList

The `ExperimentList` slot is designed to contain results from each experiment/assay. It contains a `SimpleList`.

sampleMap

The `sampleMap` contains a `DataFrame` of translatable identifiers of samples and participants or biological units. The standard column names of the `sampleMap` are "assay", "primary", and "col-name". Note that the "assay" column is a factor corresponding to the names of each experiment in the `ExperimentList`. In the case where these names do not match between the `sampleMap` and the experiments, the documented experiments in the `sampleMap` take precedence and experiments are dropped by the harmonization procedure. The constructor function will generate a `sampleMap` in the case where it is not provided and this method may be a 'safer' alternative for creating the `MultiAssayExperiment` (so long as the rownames are identical in the `colData`, if provided). An empty `sampleMap` may produce empty experiments if the levels of the "assay" factor in the `sampleMap` do not match the names in the `ExperimentList`.

coercion

Convert a list or `S4 List` to a `MultiAssayExperiment` object using the `methods::as` function.

In the following example, `x` is either a list or `List`:

```
as(x, "MultiAssayExperiment")
```

Convert a MultiAssayExperiment to MAF class object using the `methods::as` function.

In the following example, x is a MultiAssayExperiment:

```
MultiAssayExperimentToMAF(x)
```

See Also

[MultiAssayExperiment-methods](#) for slot modifying methods, [MultiAssayExperiment API](#)

Examples

```
example("MultiAssayExperiment")

## Subsetting
# Rows (i) Rows/Features in each experiment
mae[1, , ]
mae[c(TRUE, FALSE), , ]

# Columns (j) Rows in colData
mae[, rownames(colData(mae))[3:2], ]

# Assays (k)
mae[, , "Affy"]

## Complete cases (returns logical vector)
completes <- complete.cases(mae)
compMAE <- mae[, completes, ]
compMAE
colData(compMAE)

example("MultiAssayExperiment")

## Add an experiment
test1 <- mae[[1L]]
colnames(test1) <- rownames(colData(mae))

## Combine current MultiAssayExperiment with additional experiment
## (no sampleMap)
c(mae, newExperiment = test1)

test2 <- mae[[3L]]
c(mae, newExp = test2, mapFrom = 3L)

## Add experiment using experiment name in mapFrom
c(mae, RNASeqGeneV2 = test2, mapFrom = "RNASeqGene")
```

MultiAssayExperiment-helpers

A group of helper functions for manipulating and cleaning a MultiAssayExperiment

Description

A set of helper functions were created to help clean and manipulate a MultiAssayExperiment object. intersectRows also works for ExperimentList objects.

- complete.cases: Returns a logical vector corresponding to 'colData' rows that have data across all experiments
- isEmpty: Returns a logical TRUE value for zero length MultiAssayExperiment objects
- intersectRows: Takes all common rows across experiments, excludes experiments with empty rownames
- intersectColumns: A wrapper for complete.cases to return a MultiAssayExperiment with only those biological units that have measurements across all experiments
- replicated: Identifies, via logical vectors, colnames that originate from a single biological unit within each assay
- replicates: Provides the replicate colnames found with the replicated function by their name, empty list if none
- anyReplicated: Whether the assay has replicate measurements
- showReplicated: Displays the actual columns that are replicated per assay and biological unit, i.e., primary value (colData rowname) in the sampleMap
- mergeReplicates: A function that combines replicated / repeated measurements across all experiments and is guided by the replicated return value
- longFormat: A MultiAssayExperiment method that returns a small and skinny [DataFrame](#). The colDataCols arguments allows the user to append colData columns to the data.
- wideFormat: A function to reshape the data in a MultiAssayExperiment to a "wide" format [DataFrame](#). Each row in the DataFrame represents an observation (corresponding to an entry in the colData). If replicates are present, their data will be appended at the end of the corresponding row and will generate additional NA data. It is recommended to remove or consolidate technical replicates with mergeReplicates. Optional colDataCols can be added when the original object is a MultiAssayExperiment.
- hasRowRanges: A function that identifies ExperimentList elements that have a [rowRanges](#) method
- getWithColData: A convenience function for extracting an assay and associated colData
- renamePrimary: A convenience function to rename the primary biological units as represented in the rownames(colData)
- renameColname: A convenience function to rename the colnames of a particular assay

Usage

```
## S4 method for signature 'MultiAssayExperiment'
complete.cases(...)
```

```
## S4 method for signature 'MultiAssayExperiment'
isEmpty(x)
```

```
intersectRows(x)
```

```
intersectColumns(x)

replicated(x)

## S4 method for signature 'MultiAssayExperiment'
replicated(x)

anyReplicated(x)

## S4 method for signature 'MultiAssayExperiment'
anyReplicated(x)

showReplicated(x)

## S4 method for signature 'MultiAssayExperiment'
showReplicated(x)

replicates(x, ...)

## S4 method for signature 'MultiAssayExperiment'
replicates(x, ...)

mergeReplicates(x, replicates = list(), simplify = BiocGenerics::mean, ...)

## S4 method for signature 'MultiAssayExperiment'
mergeReplicates(
  x,
  replicates = replicated(x),
  simplify = BiocGenerics::mean,
  ...
)

## S4 method for signature 'ANY'
mergeReplicates(x, replicates = list(), simplify = BiocGenerics::mean, ...)

longFormat(object, colDataCols = NULL, i = 1L)

wideFormat(
  object,
  colDataCols = NULL,
  check.names = TRUE,
  collapse = "_",
  i = 1L
)

hasRowRanges(x)
```

```

## S4 method for signature 'MultiAssayExperiment'
hasRowRanges(x)

## S4 method for signature 'ExperimentList'
hasRowRanges(x)

getWithColData(x, i, mode = c("append", "replace"), verbose = FALSE)

renamePrimary(x, value)

renameColname(x, i, value)

splitAssays(x, hitList)

## S4 method for signature 'MultiAssayExperiment'
splitAssays(x, hitList)

makeHitList(x, patternList)

```

Arguments

...	Additional arguments. See details for more information.
x	A MultiAssayExperiment or ExperimentList
replicates	A list of LogicalLists indicating multiple / duplicate entries for each biological unit per assay, see replicated (default replicated(x)).
simplify	A function for merging repeat measurements in experiments as indicated by the replicated method for MultiAssayExperiment
object	Any supported class object
colDataCols	A character, logical, or numeric index for colData columns to be included
i	longFormat: The i-th assay in SummarizedExperiment-like objects. A vector input is supported in the case that the SummarizedExperiment object(s) has more than one assay (default 1L), renameColname: Either a numeric or character index indicating the assay whose colnames are to be renamed
check.names	(logical default TRUE) Column names of the output DataFrame will be checked for syntactic validity and made unique, if necessary
collapse	(character default "_") A single string delimiter for output column names. In wideFormat, experiments and rownames (and when replicate samples are present, colnames) are separated by this delimiter
mode	String indicating how MultiAssayExperiment column-level metadata should be added to the SummarizedExperiment colData.
verbose	logical(1) Whether to suppressMessages on subsetting operations in getWithColData (default FALSE)
value	renamePrimary: A character vector of the same length as the existing rownames(colData) to use for replacement, renameColname: A CharacterList or list with matching lengths to replace colnames(x)

hitList	a named list or List of logical vectors that indicate groupings in the assays
patternList	a named list or List of atomic character vectors that are the input to grepl for identifying groupings in the assays

Details

The replicated function finds replicate measurements in each assay and returns a list of [LogicalLists](#). Each element in a single [LogicalList](#) corresponds to a biological or *primary* unit as in the `sampleMap`. Below is a small graphic for one particular biological unit in one assay, where the logical vector corresponds to the number of measurements/samples in the assay:

```
> replicated(MultiAssayExperiment)
(list str)      '-- $ AssayName
(LogicalList str)  '-- [[ "Biological Unit" ]]
Replicated if sum(...) > 1      '-- TRUE TRUE FALSE FALSE
```

`anyReplicated` determines if any of the assays have at least one replicate. *Note.* These methods are not available for the `ExperimentList` class due to a missing `sampleMap` structure (by design). `showReplicated` returns a list of [CharacterLists](#) where each element corresponds to the the biological or *primary* units that are replicated in that assay element. The values in the inner list are the colnames in the assay that are technical replicates.

The `replicates` function (noun) returns the colnames from the `sampleMap` that were identified as replicates. It returns a list of [CharacterLists](#) for each assay present in the `MultiAssayExperiment` and an inner entry for each biological unit that has replicate observations in that assay.

The `mergeReplicates` function is a house-keeping method for a `MultiAssayExperiment` where only complete cases are returned. This by-assay operation averages replicate measurements (by default) and columns are aligned by the row order in `colData`. Users can provide their own function for merging replicates with the `simplify` functional argument. Additional inputs ... are sent to the 'simplify' function.

The `mergeReplicates` "ANY" method consolidates duplicate measurements for rectangular data structures, returns object of the same class (endomorph). The ellipsis or ... argument allows the user to provide additional arguments to the `simplify` functional argument.

The `longFormat` "ANY" class method, works with classes such as [ExpressionSet](#) and [SummarizedExperiment](#) as well as `matrix` to provide a consistent long and skinny [DataFrame](#).

The `hasRowRanges` method identifies assays that support a [rowRanges](#) method and return a [GRanges](#) object.

Value

See the itemized list in the description section for details.

mergeReplicates

The `mergeReplicates` function makes use of the output from `replicated` which will point out the duplicate measurements by biological unit in the `MultiAssayExperiment`. This function will return a `MultiAssayExperiment` with merged replicates. Additional arguments can be provided to the `simplify` argument via the ellipsis (...). For example, when replicates "TCGA-B" and "TCGA-A" are found in the assay, the name of the first appearing replicate is taken (i.e., "B"). Note that a

typical use case of merging replicates occurs when there are multiple measurements on the **same** sample (within the same assay) and can therefore be averaged.

longFormat

The 'longFormat' method takes data from the [ExperimentList](#) in a `MultiAssayExperiment` and returns a uniform `DataFrame`. The resulting `DataFrame` has columns indicating primary, rowname, colname and value. This method can optionally include columns of the `MultiAssayExperiment` colData named by `colDataCols` character vector argument. (`MultiAssayExperiment` method only). The `i` argument allows the user to specify the assay value for the `SummarizedExperiment` assay function's `i` argument.

wideFormat

The `wideFormat` function returns standardized wide `DataFrame` where each row represents a biological unit as in the `colData`. Depending on the data and setup, biological units can be patients, tumors, specimens, etc. Metadata columns are generated based on the names produced in the wide format `DataFrame`. These can be accessed via the `mcols()` function. See the `wideFormat` section for description of the `colDataCols` and `i` arguments.

hasRowRanges

The `hasRowRanges` method identifies assays with associated ranged row data by directly testing the method on the object. The result from the test must be a `GRanges` class object to satisfy the test.

getWithColData

The `getWithColData` function allows the user to conveniently extract a particular assay as indicated by the `i` index argument. It will also attempt to provide the `colData` along with the extracted object using the `colData<-` replacement method when possible. Typically, this method is available for `SummarizedExperiment` and `RaggedExperiment` classes.

The setting of `mode` determines how the `colData` is added. If `mode="append"`, the `MultiAssayExperiment` metadata is appended onto that of the `SummarizedExperiment`. If any fields are duplicated by name, the values in the `SummarizedExperiment` are retained, with a warning emitted if the values are different. For `mode="replace"`, the `MultiAssayExperiment` metadata replaces that of the `SummarizedExperiment`, while for `mode="none"`, no replacement or appending is performed.

rename*

The `renamePrimary` function allows the user to conveniently change the actual names of the primary biological units as seen in `rownames(colData)`. `renameColname` allows the user to change the names of a particular assay based on index `i`. `i` can either be a single numeric or character value. See `colnames<-` method for renaming multiple colnames in a `MultiAssayExperiment`.

splitAssays

The `splitAssays` method separates columns in each of the assays based on the `hitList` input. The `hitList` can be generated using the `makeHitList` helper function. To use the `makeHitList` helper, the user should input a list of patterns that will match on the column names of each assay.

These matches should be mutually exclusive as to avoid repetition of columns across assays. See the examples section.

Examples

```
example(MultiAssayExperiment)

complete.cases(mae)

isEmpty(MultiAssayExperiment())

## renaming biological units (primary)

mae2 <- renamePrimary(mae, paste0("pt", 1:4))
colData(mae2)
sampleMap(mae2)

## renaming observational units (colname)

mae2 <- renameColname(mae, i = "Affy", paste0("ARRAY", 1:4))
colnames(mae2)
sampleMap(mae2)

patts <- list(
  normals = "TCGA-[A-Z0-9]{2}-[A-Z0-9]{4}-11",
  tumors = "TCGA-[A-Z0-9]{2}-[A-Z0-9]{4}-01"
)

data("miniACC")

hits <- makeHitList(miniACC, patts)

## only tumors present
splitAssays(miniACC, hits)
```

MultiAssayExperiment-methods

Accessing and modifying information in MultiAssayExperiment

Description

A set of accessor and setter generic functions to extract either the `sampleMap`, the `ExperimentList`, `colData`, or metadata slots of a `MultiAssayExperiment` object

Usage

```
## S4 method for signature 'MultiAssayExperiment'
sampleMap(x)

## S4 method for signature 'MultiAssayExperiment'
experiments(x)

## S4 method for signature 'MultiAssayExperiment'
colData(x, ...)

## S4 method for signature 'MultiAssayExperiment'
drops(x)

## S4 replacement method for signature 'MultiAssayExperiment,DataFrame'
sampleMap(object) <- value

## S4 replacement method for signature 'MultiAssayExperiment,ANY'
sampleMap(object) <- value

drops(x, ...) <- value

## S4 replacement method for signature 'MultiAssayExperiment,ExperimentList'
experiments(object) <- value

## S4 replacement method for signature 'MultiAssayExperiment,List'
experiments(object) <- value

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

## S4 replacement method for signature 'MultiAssayExperiment,ANY'
colData(x, ...) <- value

## S4 replacement method for signature 'MultiAssayExperiment'
drops(x, ...) <- value

## S4 replacement method for signature 'MultiAssayExperiment'
x$name <- value

## S4 replacement method for signature 'MultiAssayExperiment'
names(x) <- value

## S4 replacement method for signature 'MultiAssayExperiment,List'
colnames(x) <- value

## S4 replacement method for signature 'MultiAssayExperiment,list'
colnames(x) <- value
```

```
## S4 method for signature 'MultiAssayExperiment'
x$name

## S4 method for signature 'MultiAssayExperiment'
metadata(x, ...)

## S4 replacement method for signature 'MultiAssayExperiment'
metadata(x, ...) <- value
```

Arguments

...	Argument not in use
object, x	A MultiAssayExperiment object
value	See details.
name	A column in colData

Value

Accessors: Either a sampleMap, ExperimentList, or DataFrame object

Setters: A MultiAssayExperiment object

Accessors

Eponymous names for accessing MultiAssayExperiment slots with the exception of the [ExperimentList](#) accessor named experiments.

- colData: Access the colData slot
- sampleMap: Access the sampleMap slot
- experiments: Access the [ExperimentList](#) slot
- [[: Access the [ExperimentList](#) slot
- \$: Access a column in colData
- drops: Get a vector of dropped [ExperimentList](#) names

Setters

Setter method values (i.e., 'function(x) <- value'):

- experiments<-: An [ExperimentList](#) object containing experiment data of supported classes
- sampleMap<-: A [DataFrame](#) object relating samples to biological units and assays
- colData<-: A [DataFrame](#) object describing the biological units
- metadata<-: A list object of metadata
- [[<-: Equivalent to the experiments<- setter method for convenience
- \$<-: A vector to replace the indicated column in colData
- drops<-: Trace [ExperimentList](#) names that have been removed

Examples

```
## Load example MultiAssayExperiment
example(MultiAssayExperiment)

## Access the sampleMap
sampleMap(mae)

## Replacement method for a MultiAssayExperiment sampleMap
sampleMap(mae) <- S4Vectors::DataFrame()

## Access the ExperimentList
experiments(mae)

## Replace with an empty ExperimentList
experiments(mae) <- ExperimentList()

## Access the metadata
metadata(mae)

## Replace metadata with a list
metadata(mae) <- list(runDate =
  format(Sys.time(), "%B %d, %Y"))

## Access the colData
colData(mae)

## Access a column in colData
mae$age

## Replace a column in colData
mae$age <- mae$age + 1
```

MultiAssayExperimentToMAF

Convert MultiAssayExperiment to MAF class

Description

Take a MultiAssayExperiment object with specific mutation assays and convert these into a maf tools representation. The names provided via synAssay and nonSynAssay must match exactly those assays in the MultiAssayExperiment.

Usage

```
MultiAssayExperimentToMAF(x, synAssay = "maf_syn", nonSynAssay = "maf_nonSyn")
```

Arguments

x	A MultiAssayExperiment object
synAssay	character(1) The name of the ExperimentList element in the MultiAssayExperiment that identifies synonymous variant classifications (default "maf_syn").
nonSynAssay	character(1) The name of the ExperimentList element in the MultiAssayExperiment that identifies non-synonymous variant classifications (default "maf_nonSyn").

Value

A MAF class object

See Also

?mafTools::MAF

prepMultiAssay	<i>Prepare a MultiAssayExperiment instance</i>
----------------	--

Description

The purpose of this helper function is to facilitate the creation of a [MultiAssayExperiment](#) object by detecting any inconsistencies with all types of names in either the [ExperimentList](#), the [colData](#), or [sampleMap](#).

Usage

```
prepMultiAssay(ExperimentList, colData, sampleMap, ...)
```

Arguments

ExperimentList	A list of all combined experiments
colData	A DataFrame of the phenotype data for all participants
sampleMap	A DataFrame of sample identifiers, assay samples, and assay names
...	Optional arguments for the MultiAssayExperiment constructor function such as metadata and drops.

Value

A list containing all the essential components of a [MultiAssayExperiment](#) as well as a "drops" metadata element that indicates non-matched names. The names of the resulting list correspond to the arguments of the MultiAssayExperiment constructor function.

Checks

The `prepMultiAssay` function checks that all columns in the `sampleMap` are character.

It checks that all names and lengths match in both the `ExperimentList` and in the unique assay names of the `sampleMap`.

If `ExperimentList` names and assay names only differ by case and are not duplicated, the function will standardize all names to lowercase.

If names cannot be matched between the `colname` column of the `sampleMap` and the `colnames` of the `ExperimentList`, those unmatched will be dropped and found in the "drops" element of the resulting list.

Names in the "primary" column of the `sampleMap`, will be matched to those in the `colData`. Unmatched "primary" column rows will be dropped from the `sampleMap`. Suggestions for name fixes in either the `ExperimentList` or `colnames` will be made when necessary.

Examples

```
## Run example
example("MultiAssayExperiment")

## Check if there are any inconsistencies within the different names
preparedMAE <- prepMultiAssay(ExpList, colDat, sampMap)

## Results in a list of components for the MultiAssayExperiment constructor
## function
MultiAssayExperiment(preparedMAE$experiments, preparedMAE$colData,
preparedMAE$sampleMap)

## Alternatively, use the do.call function
do.call(MultiAssayExperiment, preparedMAE)
```

reexports

Objects exported from other packages

Description

These objects are imported from other packages. Click on the function name to see their documentation.

- [S4Vectors::DataFrame](#)

Value

- `S4Vectors::DataFrame`: A `DataFrame` class object

Examples

```
DataFrame()
```

`subsetBy`*Subsetting a MultiAssayExperiment object*

Description

A set of functions for extracting and dividing a MultiAssayExperiment

Usage`subsetByRow(x, y, ...)``subsetByColData(x, y)``subsetByColumn(x, y)``subsetByAssay(x, y)``## S4 method for signature 'ExperimentList,ANY'``subsetByRow(x, y, ...)``## S4 method for signature 'ExperimentList,list'``subsetByRow(x, y)``## S4 method for signature 'ExperimentList,List'``subsetByRow(x, y)``## S4 method for signature 'ExperimentList,logical'``subsetByRow(x, y)``## S4 method for signature 'ExperimentList,list'``subsetByColumn(x, y)``## S4 method for signature 'ExperimentList,List'``subsetByColumn(x, y)``## S4 method for signature 'ExperimentList,logical'``subsetByColumn(x, y)``## S4 method for signature 'ExperimentList'``subsetByAssay(x, y)``## S4 method for signature 'MultiAssayExperiment,ANY'``subsetByColData(x, y)``## S4 method for signature 'MultiAssayExperiment,character'``subsetByColData(x, y)`

```
## S4 method for signature 'MultiAssayExperiment,ANY'
subsetByRow(x, y, ...)

## S4 method for signature 'MultiAssayExperiment,ANY'
subsetByColumn(x, y)

## S4 method for signature 'MultiAssayExperiment'
subsetByAssay(x, y)

## S4 method for signature 'MultiAssayExperiment,ANY,ANY,ANY'
x[i, j, k, ..., drop = FALSE]

## S4 method for signature 'MultiAssayExperiment,ANY,ANY'
x[[i, j, ...]]

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

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

Arguments

x	A <code>MultiAssayExperiment</code> or <code>ExperimentList</code>
y	Any argument used for subsetting, can be a character, logical, integer, list or List vector
...	Additional arguments passed on to lower level functions.
i	Either a character, integer, logical or <code>GRanges</code> object for subsetting by rows
j	Either a character, logical, or numeric vector for subsetting by colData rows. See details for more information.
k	Either a character, logical, or numeric vector for subsetting by assays
drop	logical (default <code>FALSE</code>) whether to drop all empty assay elements in the <code>ExperimentList</code>
value	An assay compatible with the <code>MultiAssayExperiment</code> API

Details

Subsetting a `MultiAssayExperiment` by the `j` index can yield a call to either `subsetByColData` or `subsetByColumn`. For vector inputs, the subset will be applied to the `colData` rows. For `List`-type inputs, the `List` will be applied to each of the elements in the `ExperimentList`. The order of the subsetting elements in the `List` must match that of the `ExperimentList` in the `MultiAssayExperiment`.

- `subsetByColData`: Select biological units by vector input types
- `subsetByColumn`: Select observations by assay or for each assay
- `subsetByRow`: Select rows by assay or for each assay
- `subsetByAssay`: Select experiments

Value

subsetBy* operations are endomorphic and return either MultiAssayExperiment or ExperimentList depending on the input.

Examples

```
## Load the example MultiAssayExperiment
example("MultiAssayExperiment")

## Using experiment names
subsetByAssay(mae, "Affy")

## Using numeric indices
subsetByAssay(mae, 1:2)

## Using a logical vector
subsetByAssay(mae, c(TRUE, FALSE, TRUE))

## Subset by character vector (Jack)
subsetByColData(mae, "Jack")

## Subset by numeric index of colData rows (Jack and Bob)
subsetByColData(mae, c(1, 3))

## Subset by logical indicator of colData rows (Jack and Jill)
subsetByColData(mae, c(TRUE, TRUE, FALSE, FALSE))

subsetByColumn(mae, list(Affy = 1:2,
  Methyl450k = c(3,5,2), RNASeqGene = 2:4, GISTIC = 1))

subsetWith <- S4Vectors::mendoapply(`[,`, colnames(mae),
  MoreArgs = list(1:2))
subsetByColumn(mae, subsetWith)

## Use a GRanges object to subset rows where ranged data present
egr <- GenomicRanges::GRanges(seqnames = "chr2",
  IRanges::IRanges(start = 11, end = 13), strand = "-")
subsetByRow(mae, egr)

## Use a logical vector (recycling used)
subsetByRow(mae, c(TRUE, FALSE))

## Use a character vector
subsetByRow(mae, "ENST00000355076")
```


Description

Create a generalized Venn Diagram analog for sample membership in multiple assays, using the upset algorithm in UpSetR

Usage

```
upsetSamples(
  MultiAssayExperiment,
  nsets = NULL,
  sets = names(MultiAssayExperiment),
  nintersects = NA_integer_,
  order.by = "freq",
  check.names = FALSE,
  ...
)
```

Arguments

MultiAssayExperiment	A MultiAssayExperiment object
nsets	numeric(1) The number of sets to analyze. If specified, sets will be ignored.
sets	character() A character vector of names in MultiAssayExperiment to use. If specified, nsets will be ignored.
nintersects	numeric(1) The number of intersections to plot. By default, all intersections will be plotted.
order.by	How the intersections in the matrix should be ordered by. Options include frequency (entered as "freq"), degree, or both in any order.
check.names	logical(1) Whether to munge names as in the data.frame() constructor (default FALSE).
...	parameters passed to UpSetR::upset

Value

Produces a visualization of set intersections using the UpSet matrix design

Note

This function is intended to provide convenient visualization of assay availability configurations in MultiAssayExperiment instances. The UpSetR::upset function requires data.frame input and has many parameters to tune appearance of the result. Assay name handling is important for interpretability.

Author(s)

Vincent J Carey

Examples

```
data(miniACC)
upsetSamples(miniACC)
upsetSamples(miniACC, nsets = 3, nintersects = 3)
```

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