Package: mutSignatures (via r-universe)

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Type Package

Title Decipher Mutational Signatures from Somatic Mutational Catalogs

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Author Damiano Fantini, Vania Vidimar, Joshua J Meeks

Maintainer Damiano Fantini <damiano.fantini@gmail.com>

Description Cancer cells accumulate DNA mutations as result of DNA damage and DNA repair processes. This computational framework is aimed at deciphering DNA mutational signatures operating in cancer. The framework includes modules that support raw data import and processing, mutational signature extraction, and results interpretation and visualization. The framework accepts widely used file formats storing information about DNA variants, such as Variant Call Format files. The framework performs Non-Negative Matrix Factorization to extract mutational signatures explaining the observed set of DNA mutations. Bootstrapping is performed as part of the analysis. The framework supports parallelization and is optimized for use on multi-core systems. The software was described by Fantini D et al (2020) <doi:10.1038/s41598-020-75062-0> and is based on a custom R-based implementation of the original MATLAB WTSI framework by Alexandrov LB et al (2013) <doi:10.1016/j.celrep.2012.12.008>.

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Depends R (>= 3.5), foreach

Imports graphics, stats, cluster, doParallel, ggplot2, pracma, proxy, methods

Suggests dplyr, reshape2, kableExtra, gridExtra, knitr, rmarkdown

VignetteBuilder knitr

Encoding UTF-8

LazyData true

URL https://www.data-pulse.com/dev_site/mutsignatures/

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Contents

`mutSignatures-package` *Decipher Mutational Signatures from Somatic Mutational Catalogs.*

Description

Cancer cells accumulate DNA mutations as result of DNA damage and DNA repair pro-cesses. mutSignatures is a computational framework that is aimed at deciphering DNA mutational signatures oper-ating in cancer. The input is a numeric matrix of DNA mutation counts de-tected in a panel of cancer samples. The framework performs Non-negative Matrix Factorization to extract mutational signatures explaining the observed set of DNA mutations. The framework relies on parallelization and is optimized for use on multi-core systems. This framework was described by Fantini D et al (2020) https://www.nature.com/articles/s41598-020-75062-0/ and is built upon a custom R-based implementation of the original MATLAB WTSI frame-work by Alexandrov LB et al (2013) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588146/. The mutSignatures framework has been described in peer-reviewed publications, including Fantini D et al (2018) https://www.nature.com/articles/s41388-017-0099-6/ and Fantini D et al (2019) https://www.sciencedirect.com/science/article/abs/pii/S1078143918303818/. The framework includes three modules that support raw data import and pre-processing, mutation counts deconvolution, and data visualization.

References

More info, examples and vignettes:

1. **GitHub Repo**: https://github.com/dami82/mutSignatures/
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **2020 Sci Rep paper** describing the latest version of mutSignatures: https://www.nature.com/articles/s41598-020-75062-0/

4. **Oncogene paper**: Mutational Signatures operative in bladder cancer: https://www.nature.com/articles/s41388-017-0099-6/

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as.data.frame,mutationCounts-method
Convert a mutationCounts object to data.frame.

Description

Coerce a mutationCounts-class object to data.frame by applying the coerceObj method.

Usage

```
## S4 method for signature 'mutationCounts'
as.data.frame(x)
```

Arguments

x	a mutationCounts object

---

as.data.frame,mutationSignatures-method
Convert a mutationSignatures object to data.frame.

Description

Coerce a mutationSignatures-class object to data.frame by applying the coerceObj method.

Usage

```
## S4 method for signature 'mutationSignatures'
as.data.frame(x)
```

Arguments

x	a mutationSignatures object

as.data.frame,mutSignExposures-method

Convert and/or transpose a mutSignExposures object to data.frame.

Description

Coerce a mutSignExposures-class object to data.frame by applying the coerceObj method. The data.frame can be returned in a transposed or non-transposed format.

Usage

```
## S4 method for signature 'mutSignExposures'
as.data.frame(x, row.names = NULL, optional = NULL, ...)
```

Arguments

x	a mutSignExposures object
row.names	NULL, not used
optional	NULL, not used
...	additional parameters to be passed to coerceObj, such as transpose (logical)

as.list,mutationSignatures-method

Convert a mutationSignatures object to list.

Description

Coerce a mutationSignatures-class object to list by applying the coerceObj method.

Usage

```
## S4 method for signature 'mutationSignatures'
as.list(x)
```

Arguments

x	a mutationSignatures object

---

as.list,mutFrameworkParams-method
Convert a mutFrameworkParams object to list.

Description

Coerce a mutFrameworkParams-class object to list by applying the coerceObj method.

Usage

```
## S4 method for signature 'mutFrameworkParams'
as.list(x)
```

Arguments

x	a mutFrameworkParams object

---

as.matrix,mutationCounts-method
Convert a mutationCounts object to matrix.

Description

Coerce a mutationCounts-class object to matrix by applying the coerceObj method.

Usage

```
## S4 method for signature 'mutationCounts'
as.matrix(x)
```

Arguments

x	a mutationCounts object

as.mutation.counts *Method as.mutation.counts.*

Description

Cast a data.frame into a mutationCounts-class object.

Usage

```
as.mutation.counts(x, rownames = NULL, colnames = NULL)

## S4 method for signature 'data.frame'
as.mutation.counts(x, rownames = NULL, colnames = NULL)
```

Arguments

x	an object to extract Signature Identifiers from, i.e. a mutSignExposures-class
rownames	character vector to overwrite data row names. Can be NULL if rownames(x) is not NULL.
colnames	character vector to overwrite data column names. Can be NULL if colnames(x) is not NULL.

as.mutation.signatures *Method as.mutation.signatures.*

Description

Cast a data.frame into a mutationSignatures-class object.

Usage

```
as.mutation.signatures(x)

## S4 method for signature 'data.frame'
as.mutation.signatures(x)
```

Arguments

x	a data.frame to be converted to a mutationSignatures-class object.

as.mutsign.exposures *Method as.mutsign.exposures.*

Description

Cast a data.frame into a mutSignExposures-class object.

Usage

```
as.mutsign.exposures(x, samplesAsCols = TRUE)

## S4 method for signature 'data.frame,logical'
as.mutsign.exposures(x, samplesAsCols = TRUE)
```

Arguments

x	a data.frame to be converted to a mutSignExposures-class object.
samplesAsCols	logical, are samples listed as columns in the input data.frame. If FALSE, samples are expected to be listed as rows in the input data.frame

attachContext *Attach Nucleotide Context.*

Description

Retrieve the nucleotide context around each DNA variant based on the genomic coordinates of the variant and a reference BSGenome database.

Usage

```
attachContext(
  mutData,
  BSGenomeDb,
  chr_colName = "chr",
  start_colName = "start_position",
  end_colName = "end_position",
  nucl_contextN = 3,
  context_colName = "context",
  skip_seqName_check = FALSE
)
```

Arguments

mutData	data.frame storing mutation data
BSGenomeDb	a BSGenomeDb-class object, storing info about the genome of interest
chr_colName	string, name of the column storing seqNames. Defaults to "chr"
start_colName	string, name of the column storing start positions. Defaults to "start_position"
end_colName	string, name of the column storing end positions. Defaults to "end_position"
nucl_contextN	integer, the span of nucleotides to be retrieved around the variant. Defaults to 3
context_colName	string, name of the column that will be storing the nucleotide context. Defaults to "context"
skip_seqName_check	logical, shall seqNames be checked to remove non-official chromosomes. Defaults to FALSE

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a modified data.frame including the nucleotide context in a new column

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **GitHub Repo**: https://github.com/dami82/mutSignatures/
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Sci Rep paper**, introducing mutS: https://www.nature.com/articles/s41598-020-75062-0/
4. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

`attachMutType` *Attach Mutation Types.*

Description

Modify a data.frame carrying information about DNA mutation, and add a new column that stores formatted multi-nucleotide types.

Usage

```
attachMutType(
  mutData,
  ref_colName = "reference_allele",
  var_colName = "variant_allele",
  var2_colName = NULL,
  context_colName = "context",
  format = 1,
  mutType_dict = "alexa",
  mutType_colName = "mutType"
)
```

Arguments

`mutData`	data.frame including information about DNA mutations
`ref_colName`	string, pointing to the column with information about the sequence of the "reference_allele"
`var_colName`	string, pointing to the column with information about the sequence of the "variant_allele"
`var2_colName`	string (optional), pointing to the column with information about the sequence of a second "variant_allele". Can be NULL
`context_colName`	string, pointing to the column with information about the nucleotidic "context"
`format`	integer, indicates the desired mutation type format: (1) N[R>V]N; (2) NN.R>V; (3) R.V[NRN][NVN]
`mutType_dict`	string, indicates the dictionary to be used for simplifying reverse-complement identical mutation types. It is recommended to use the standard dictionary from COSMIC, by selecting the default value, i.e. "alexa".
`mutType_colName`	string, column name of the new column added to the data.frame where mutTypes are stored.

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a data.frame including a new column with mutation Types.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- data.frame(REF = c("A", "T", "G"),
                VAR = c("G", "C", "C"),
                CTX = c("TAG", "GTG", "CGA"),
                stringsAsFactors = FALSE)
mutSignatures::attachMutType(mutData = A, ref_colName = "REF",
                             var_colName = "VAR", context_colName = "CTX")
```

---

cbind2 *Combine two mutationSignatures-class objects.*

Description

Combine two mutationSignatures-class objects.

Usage

```
## S4 method for signature 'mutationSignatures,mutationSignatures'
cbind2(x, y)
```

Arguments

x	the first mutSignExposures-class object to combine
y	the first mutSignExposures-class object to combine

Details

a variant of this method accepting more than 2 object to combine together is under preparation and be available soon...

coerceObj *Method coerceObj.*

Description

Cast an object to a different format, by extracting and returning the most appropriate information. Note that data.frames can be coerced to one of the classes defined in the mutSignatures package using coerceObj.

Usage

```
coerceObj(x, to, ...)

## S4 method for signature 'mutFrameworkParams,character'
coerceObj(x, to)

## S4 method for signature 'mutationSignatures,character'
coerceObj(x, to)

## S4 method for signature 'mutationCounts,character'
coerceObj(x, to, ...)

## S4 method for signature 'mutSignExposures,character'
coerceObj(x, to, ...)

## S4 method for signature 'data.frame,character'
coerceObj(x, to, ...)
```

Arguments

x	an object to coerce to a different format
to	string, indicates the expected format (such as list or data.frame)
...	additional parameters passed to the functions used for the coercion

countMutTypes *Count Mutation Types.*

Description

Analyze a table (data.frame) including mutation counts. Count and aggregate Count Mutation Types. If multiple samples are included in the same table, results are aggregated by samples.

Usage

```
countMutTypes(mutTable, mutType_colName = "mutType", sample_colName = NULL)
```

Arguments

mutTable	data.frame including mutation types and an optional sample ID column
mutType_colName	string, name of the column storing mutTypes
sample_colName	string, name of the column storing sample identifiers. Can be NULL

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a mutationCounts-class object

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
x <- mutSignatures:::getTestRunArgs("countMutTypes")
x
y <- mutSignatures::countMutTypes(mutTable = x,
                                  mutType_colName = "mutation",
                                  sample_colName = "sample")
y
```

`decipherMutationalProcesses` *Decipher Mutational Processes Contributing to a Collection of Genomic Mutations.*

Description

Decipher Mutational ProCancer cells accumulate DNA mutations as result of DNA damage and DNA repair processes. Thiscomputational framework allows to decipher mutational processes from cancer-derived somatic mutational catalogs.

Usage

```
decipherMutationalProcesses(input, params)
```

Arguments

`input`	a mutationCounts-class object, including a mutation counts data.
`params`	a mutFrameworkParams-class object including all the parameters required for running the mutational signature analysis.

Details

This is one of the core functions included in the original mutSignatures R library, and in the WTSI MATLAB framework. This is the main user interface for the mutSignatures analysis.

Value

list including all results of the analysis. The extracted signatures (processes) are included in the "processes" element of the list. The relative contribution of each signature in each sample is summarized in the "exposures" element.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6
4. WTSI framework: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588146/

Examples

```
library(mutSignatures)
x <- mutSignatures:::getTestRunArgs("decipherMutationalProcesses")
x$muts
y <- mutSignatures::decipherMutationalProcesses(input = x$muts,
                                                params = x$params)
y$Results$signatures
```

`extractXvarlinkData` *Extract Variants from XvarlinkData.*

Description

Extract Variants from data stored as XvarlinkData.

Usage

```
extractXvarlinkData(xvarLink_data)
```

Arguments

`xvarLink_data`	character vector, including mutation data embedded in XvarlinkData

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a data.frame including mutations as well as corresponding reference nucleotides.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
x <- mutSignatures:::getTestRunArgs("extractXvarlinkData")
y <- mutSignatures:::extractXvarlinkData(xvarLink_data = x)
y
```

`filterSNV` *Filter Single Nucleotide Variants.*

Description

Remove entries corresponding to non-SNV, such as insertions and deletions.

Usage

```
filterSNV(dataSet, seq_colNames)
```

Arguments

`dataSet`	data.frame including variant information
`seq_colNames`	character vector with the names of the columns storing variant data

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a filtered data.frame only including SNVs

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
x <- mutSignatures:::getTestRunArgs("filterSNV")
nrow(x)
y <- mutSignatures::filterSNV(dataSet = x,
                              seq_colNames = c("REF", "ALT"))
nrow(y)
```

`frequencize` *Convert Mutation COunts to PerMille Frequencies.*

Description

Convert Mutation COunts to frequencies. Typically, a permille frequence is returned. In other words, the resulting number indicates the expected mutation count if the genome hat a total of 1000 mutations. This way, the MutSignatures analysis will be less biased toward the hyper-mutator samples.

Usage

```
frequencize(countMatrix, permille = TRUE)
```

Arguments

`countMatrix`	numeric matrix of mutation counts
`permille`	ligucal, shall the permille conversion be used instead of the standard frequency

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

list including colSums (mutation burden of each sample) and freqs (matrix of frequencies)

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
2. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- cbind(c(7, 100, 90, 1000), c(1, 3, 5, 9))
fA <- mutSignatures::frequencize(A)
fA$freqs
```

`getCosmicSignatures` *Obtain COSMIC mutational Signatures.*

Description

Obtain latest mutational Signature definitions from COSMIC. FOr more info, please visit: http://cancer.sanger.ac.uk/

Usage

```
getCosmicSignatures(forceUseMirror = FALSE, asMutSign = TRUE)
```

Arguments

`forceUseMirror`	logical, shall signatures be downloaded from a mirror. Set to TRUE if the COSMIC server goes down.
`asMutSign`	logical, shall data be returned as a mutSignatures-class object. Defaults to TRUE

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

an object storing COSMIC mutational signature data

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

getCounts *Method getCounts.*

Description

Retrieve mutation counts from an object.

Usage

```
getCounts(x)

## S4 method for signature 'mutationCounts'
getCounts(x)
```

Arguments

x	an object to extract Mutation counts from, i.e. a mutationCounts-class object

getFwkParam *Method getFwkParam.*

Description

Retrieve the list of parameters used for running a Mutation Signature Analysis.

Usage

```
getFwkParam(x, label)

## S4 method for signature 'mutFrameworkParams,character'
getFwkParam(x, label)
```

Arguments

x	a mutFrameworkParams-class object
label	string, corresponding to the parameter name to extract

getMutationTypes *Method getMutationTypes.*

Description

Retrieve the list of mutation types from an object.

Usage

```
getMutationTypes(x)

## S4 method for signature 'mutationSignatures'
getMutationTypes(x)

## S4 method for signature 'mutationCounts'
getMutationTypes(x)
```

Arguments

x	an object to extract Mutation types from, i.e. a mutationSignatures-class or a mutationCounts-class object

getSampleIdentifiers *Method getSampleIdentifiers.*

Description

Retrieve the list of sample identifiers from an object.

Usage

```
getSampleIdentifiers(x)

## S4 method for signature 'mutationCounts'
getSampleIdentifiers(x = "mutationCounts")

## S4 method for signature 'mutSignExposures'
getSampleIdentifiers(x)
```

Arguments

x	an object to extract Mutation types from, i.e. a mutationCounts-class or a mutSignExposures-class object

getSignatureIdentifiers *Method getSignatureIdentifiers.*

Description

Retrieve the list of signature identifiers from an object.

Usage

```
getSignatureIdentifiers(x)

## S4 method for signature 'mutSignExposures'
getSignatureIdentifiers(x)

## S4 method for signature 'mutationSignatures'
getSignatureIdentifiers(x)
```

Arguments

x	an object to extract Signature Identifiers from, i.e. a mutSignExposures-class or a mutationSignatures-class object

importVCFfiles *Import Mutation data from VCF files.*

Description

Import Mutation data from VCF files. The first 8 columns are expected in the following order: c("CHROM", "POS", "ID", "REF", "ALT", "QUAL", "FILTER", "INFO"). Optional columns can be present to inform about sample ID or other info.

Usage

```
importVCFfiles(vcfFiles, sampleNames = NULL, sampleNameColumn = "SAMPLEID")
```

Arguments

vcfFiles	character vector, includes the names of the VCF files to be analyzed
sampleNames	character vector with alternative sample names (otherwise, VCF file names will be used as sample identifiers)
sampleNameColumn	string, name of the column that will be added to inform about the sample ID where each variant wes identified

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a concatenated data.frame with all variants found in the input VCF files. Sample ID is stored in the column selected via the ‘sampleNameColumn‘ argument.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

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matchSignatures *Match Mutational Signatures.*

Description

Analyze the similarity between mutational signatures from different analyses/runs. This function can be helpful to match de novo extracted signatures with previously described signatures (such as COSMIC), or to reveal signatures that can be identified with alternative NMF algorithms, or that may be due to an algorithm bias.

Usage

```
matchSignatures(
  mutSign,
  reference = NULL,
  method = "cosine",
  threshold = 0.5,
  plot = TRUE
)
```

Arguments

mutSign	a mutationSignatures object
reference	a mutationSignatures object. If NULL, COSMIC signatures will be retrieved
method	distance method used to compute similarity (1 - distance)
threshold	signal (similarity) upper threshold for maxing the signal
plot	logical, shall a heatmap be plotted

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

list, including distance matrix and a heatmap plot

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

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msigPlot *Method msigPlot.*

Description

Generate standard plots using data from mutsignature-class objects.

Usage

```
msigPlot(x, ...)

## S4 method for signature 'mutationSignatures'
msigPlot(x, ...)

## S4 method for signature 'mutationCounts'
msigPlot(x, ...)
```

```
## S4 method for signature 'mutSignExposures'
msigPlot(x, ...)
```

Arguments

x	a mutSignatures object
...	additional parameters, including standard graphical parameters, as well as a set of class-specific arguments: * x is a mutationSignatures object: - signature, numeric; numeric index of the signature to display - main, string; title of the plot * x is a mutationCounts object - sample, numeric or string, i.e. the identifier or the index of the sample to be plotted - main, string, title of the plot * x is a mutSignExposures object - top, integer, the maximum number of samples to be plotted

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mutationCounts-class *Class mutationCounts.*

Description

Class mutationCounts defines objects storing Mutation COunts data.

Usage

```
## S4 method for signature 'mutationCounts'
initialize(.Object, x, muts, samples)
```

Arguments

.Object	the mutationCounts object being built
x	data.frame including mutation count values for each biological sample
muts	data.frame including information about mutation types
samples	data.frame including information about sample identifiers (unique names)

Slots

`counts` data.frame including information about mutation counts

`mutTypes` data.frame including information about mutation types

`sampleId` data.frame including information about sample identifiers

Author(s)

Damiano Fantini <damiano.fantini@gmail.com>

mutationSignatures-class
Class mutationSignatures.

Description

Class mutationSignatures defines objects storing Mutational Signatures data.

Usage

```
## S4 method for signature 'mutationSignatures'
initialize(.Object, x, muts, signNames)
```

Arguments

.Object	the mutationSignatures object being built
x	data.frame including fequency data of multiple mutation signatures
muts	data.frame including information about mutation types
signNames	data.frame including information about mutation signature names (unique identifiers)

Slots

mutationFreq data.frame including information about mutation frequencies

mutTypes data.frame including information about mutation types

signatureId data.frame including information about mutation signature Identifiers

Author(s)

Damiano Fantini <damiano.fantini@gmail.com>

mutFrameworkParams-class
Class mutFrameworkParams.

Description

Class mutFrameworkParams defines objects including the set of parameters used for running a Mutational Signature Analysis.

Usage

```
## S4 method for signature 'mutFrameworkParams'
initialize(.Object, params)
```

Arguments

.Object	the mutFrameworkParams object being built
params	list including values for a set of mutFramework params

Slots

params list including the set of parameters used for running a Mutational Signature Analysis

Author(s)

Damiano Fantini <damiano.fantini@gmail.com>

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mutSigData *Input Data and Examples for Running Mutational Signatures Analyses*

Description

A series of objects, including collections of DNA mutations from 50 Bladder cancer samples, as well as mutational signatures extracted from the same samples. Mutation catalogs were obtained from a TCGA bladder cancer dataset (data available from the BROAD Institute). Original sample IDs were shuffled and then re-encoded. Data are available in different formats, and can be used as input for running mutational signature analyses.

Usage

```
data("mutSigData")
```

Format

A list with 6 elements. Each element is a different type of mutSignatures input/data:

inputA data.frame with 10401 rows and 4 columns. DNA mutation data mimicking a TCGA dataset downloaded using TCGAretriever/cBio

inputB data.frame with 13523 rows and 12 columns. DNA mutation data mimicking a TCGA MAF file

inputC data.frame with 13523 rows and 11 columns. DNA mutation data mimicking a VCF file decorated with a SAMPLEID column

inputC.ctx data.frame with 13523 rows and 11 columns. DNA mutation data mimicking a VCF file decorated with a SAMPLEID column

inputD data.frame with 13487 rows and 56 columns. DNA mutation data mimicking a set of VCF files casted into a 2D matrix (samples as columns)

inputS list including data for silhouette plot generation (used in the vignette)

blcaMUTS data.frame with 96 rows and 50 columns. A table of DNA mutation counts (rows are mutation types; columns are samples)

blcaSIGS data.frame with 96 rows and 8 columns. Set of 8 mutational signatures (rows are mutation types; columns are signatures)

.addON list of add-on functions (executed only upon request, not evaluated; these may require manual installation of external libraries from Bioconductor or GitHUB)

Details

Examples and more information are available in the vignette, as well as at the following URL: https://www.data-pulse.com/dev_site/mutsignatures/

Source

BLCA data were downloaded from http://gdac.broadinstitute.org/ and then further processed, modified, and formatted.

Examples

```
data(mutSigData)
print(mutSigData$input.A[1:6,])
```

---

mutSignExposures-class

Class mutSignExposures.

Description

Class mutSignExposures defines objects storing information about Exposures of biological samples to Mutational Signatures.

Usage

```
## S4 method for signature 'mutSignExposures'
initialize(.Object, x, samples, signNames)
```

Arguments

.Object	the mutSignExposures object being built
x	data.frame including numeric values of exposures to mutational signatures
samples	data.frame including information about biological sample identifiers (unique names)
signNames	data.frame including information about mutational signature identifiers

Slots

exposures data.frame including information about exposures

sampleId data.frame including information about sample identifiers

signatureId data.frame including information about signature identifiers

Author(s)

Damiano Fantini <damiano.fantini@gmail.com>

`plotMutTypeProfile` *Plot Mutation Signature Profiles.*

Description

Build a barplot to visualize the relative abundance of mutation counts in a mutational signature or biological sample of interest.

Usage

```
plotMutTypeProfile(
  mutCounts,
  mutLabs,
  freq = TRUE,
  ylim = "auto",
  ylab = "Fraction of Variants",
  xlab = "Sequence Motifs",
  xaxis_cex = 0.475,
  cols = c("#4eb3d3", "#040404", "#b30000", "#bdbdbd", "#41ab5d", "#dd3497"),
  main = "MutType Profile"
)
```

Arguments

`mutCounts`	data.frame including mutation types counts or frequencies, such as a data.frame of mutation counts from samples, or mutation type frequencies from a mutational signature.
`mutLabs`	character vector, labels to be used for the mutation types
`freq`	logical, shall frequency be plotted rather than counts. Defaults to TRUE
`ylim`	values used for ylim. Defaults to "auto" (ylim automatically set)
`ylab`	string, used as y-axis title. Defaults to "Fraction of Variants"
`xlab`	string, used as x-axis title. Defaults to "Sequence Motifs"
`xaxis_cex`	numeric, cex value for the xaxis
`cols`	character vector, indicates the colors to be used for the bars. It typically requires 6 colors.
`main`	string, tutle of the plot. Defaults to "MutType Profile"

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

NULL. A plot is printed to the active device.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

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plotSignExposures *Plot Signature Exposure Profiles.*

Description

Build a barplot to visualize exposures to mutation signatures.

Usage

```
plotSignExposures(mutCount, top = 50)
```

Arguments

mutCount	a data.frame including mutation Counts
top	integer, max number of samples to include in the plot

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a plot (ggplot2 object)

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
2. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

`prelimProcessAssess` *Run a Preliminary Process Assess analysis.*

Description

This function is an attempt to analyze the relationship between error and k. In other words, the goal of prelimProcessAssess is to visualize the reduction in the error/residuals

Usage

```
prelimProcessAssess(
  input,
  maxProcess = 6,
  approach = "counts",
  plot = TRUE,
  verbose = TRUE
)
```

Arguments

`input`	a mutationCounts-class object
`maxProcess`	integer, maximum k to test
`approach`	sting, "counts" or "freq"
`plot`	logical, shall a plot be printed to the active device
`verbose`	logical, info about the ongoing analysis be messaged/printed to console

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a data.frame showing the estimated total error with respect to the range of k values

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

`processVCFdata` *Process VCF data.*

Description

Check, annotate, and process variants imported from a list of VCF files, so that it can be used to run a mutational signature analysis

Usage

```
processVCFdata(
  vcfData,
  BSGenomeDb,
  chr_colName = "CHROM",
  pos_colName = "POS",
  ref_colName = "REF",
  alt_colName = "ALT",
  sample_colName = NULL,
  nucl_contextN = 3,
  verbose = TRUE
)
```

Arguments

`vcfData`	data.frame, includes mutation data from 2 or more samples
`BSGenomeDb`	a BSGenomeDb-class object storing the genomic sequences and coordinates
`chr_colName`	string, name of the column including the chromosome (seq) name. Defaults to "CHROM"
`pos_colName`	string, name of the column including the genomic coordinates/position. Defaults to "POS"
`ref_colName`	string, name of the column including the reference nucleotide. Defaults to "REF"
`alt_colName`	string, name of the column including the variant nucleotide. Defaults to "ALT"
`sample_colName`	string, name of the column including the sample ID. Can be NULL
`nucl_contextN`	integer, span (in nucelotides) of the context around the variants. Defaults to 3
`verbose`	logical, shall information about the ongoing analysis be printed to console

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a data.frame including processed variants from VCF files

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

---

removeMismatchMut *Remove Mismatched Mutations.*

Description

Remove mutation types that do not match the expected nucleotidic context.

Usage

```
removeMismatchMut(
  mutData,
  refMut_colName = "mutation",
  context_colName = "context",
  refMut_format = "N>N"
)
```

Arguments

mutData	data.frame including mutation data, as well as the nucleotide context around the mutated position
refMut_colName	string, name of the column storing REF and VAR data. Defaults to "N>N"
context_colName	string, name of the column storing nucleotide context around the variant.
refMut_format	string, format of mutation types. Defaults to "N>N"

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

filtered data.frame

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
x <- mutSignatures:::getTestRunArgs("removeMismatchMut")
y <- mutSignatures:::removeMismatchMut(x,
                                       refMut_colName = "REF",
                                       context_colName = "context",
                                       refMut_format = "N")
y
```

---

resolveMutSignatures *Resolve Mutation Signatures.*

Description

If Mutation signatures are known (such as COSMIC signatures), we can estimate the contribution of each signature in different samples. This functions used a matrix of mutation counts and a matrix of mutation signatures, and estimates Exposures to Mutational Signature of each sample.

Usage

```
resolveMutSignatures(mutCountData, signFreqData, byFreq = TRUE)
```

Arguments

mutCountData	object storing mutation counts
signFreqData	object storing mutation signatures
byFreq	logical, shall exposures be estimated on per_mille normalized counts

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a list of objects including data about exposures to mutational signatures

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
x <- mutSignatures:::getTestRunArgs("resolveMutSignatures")
y <- mutSignatures::resolveMutSignatures(mutCountData = x$muts, signFreqData = x$sigs)
y
```

---

revCompl *Compute Reverse Complement sequences.*

Description

Transform a DNA sequence into its reverse-complement sequence. ALternatively, only the reverse sequence (or only the complement) can be returned.

Usage

```
revCompl(DNAseq, rev = TRUE, compl = TRUE)
```

Arguments

DNAseq	character vector of DNA sequences
rev	logical, shall the reverse sequence be computed
compl	logical, shall the complementary sequence be computed

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

a character vector including transformed DNA sequences

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- c("TAACCG", "CTCGA", "CNNA")
mutSignatures::revCompl(A)
```

---

setFwkParam *Method setFwkParam.*

Description

Set or update one of the parameters in a mutFrameworkParams-class object. Individual paramaters can be set or updated, by passing the parameter label, and the corresponding parameter value.

Usage

```
setFwkParam(x, label, value)

## S4 method for signature 'mutFrameworkParams,character'
setFwkParam(x, label, value)
```

Arguments

x	an object to extract Signature Identifiers from, i.e. a mutSignExposures-class
label	string corresponding to the parameter label to be updated
value	new value (string or numeric) of the parameter to be updated

---

setMutClusterParams *Set Parameters for Extracting Mutational Signatures.*

Description

Create an object including all parameters required for running the mutSignatures framework.

Usage

```
setMutClusterParams(
  num_processesToExtract = 2,
  num_totIterations = 10,
  num_parallelCores = 1,
  thresh_removeWeakMutTypes = 0.01,
  thresh_removeLastPercent = 0.07,
  distanceFunction = "cosine",
  num_totReplicates = 100,
  eps = 2.2204e-16,
  stopconv = 20000,
  niter = 1e+06,
  guided = TRUE,
  debug = FALSE,
  approach = "freq",
  stopRule = "DF",
  algorithm = "brunet",
  logIterations = "lite",
  seed = 12345
)
```

Arguments

num_processesToExtract	integer, number of mutational signatures to extract
num_totIterations	integer, total number of iterations (bootstrapping)
num_parallelCores	integer, number of cores to use for the analysis
thresh_removeWeakMutTypes	numeric, threshold for filtering out under-represented mutation types
thresh_removeLastPercent	numeric, threshold for removing outlier iteration results

`distanceFunction`
: string, method for calculating distances. Default method is "cosine"

`num_totReplicates`
: integer, number of replicates while checking stability

`eps`
: numeric, close-to-zero positive numeric value for replacing zeros and preventing negative values to appear in the matrix during NMF

`stopconv`
: integer, max number of stable iterations before termination. Defaults to 20000.

`niter`
: integer, max number of iterations to run. Defaults to 1000000

`guided`
: logical, shall clustering be guided to improve aggregation upon bootstrapping

`debug`
: logical, shall the analysis be run in DEBUG mode

`approach`
: string, indicating whether to model absolute counts ("counts") or per_mille frequency ("freq"). Defaults to "freq".

`stopRule`
: = string, use the sub-optimal termination rule ("AL") from the WTSI package (actually, iterations won't terminate, so niter will most certainly reached) or our efficient termination rule ("DF"). Defaults to "DF". The "AL" option is implemented for compatibility reasons, but not recommended.

`algorithm`
: string, algorithm to be used for NMF. Set to "brunet", or "alexa" for using the standard algorithm (Brunet's), otherwise the alternative "chihjen" algorithm will be used.

`logIterations`
: string indicating if storing and returining all intermediates, or only final results. Defaults to "lite", i.e. returns full output and limited intermediates. Alternatively, set to "full".

`seed`
: integer, seed to set for reproducibility

Value

Object including all parameters for running the analysis

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6
4. WTSI framework: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588146/

Examples

```
library(mutSignatures)
# defaults params
A <- setMutClusterParams()
A
# A second example, set num_processes
B <- setMutClusterParams(num_processesToExtract = 5)
B
```

`setSignatureNames` *Method setSignatureNames.*

Description

Update signature names of a Mutation Signatures object.

Usage

```
setSignatureNames(x, names)

## S4 method for signature 'mutationSignatures,character'
setSignatureNames(x, names)
```

Arguments

`x`	a mutationSignatures object
`names`	character vector, these are the new names that will be assigned to the signatures.

`show,mutationCounts-method`
Show method of the mutationCounts Class.

Description

Show method of the mutationCounts Class.

Print method of the mutationCounts Class.

Usage

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

## S4 method for signature 'mutationCounts'
print(x)
```

Arguments

object	the mutationCounts object being shown
x	the mutationCounts object being printed

---

show,mutationSignatures-method

Show method of the mutationSignatures Class.

Description

Show method of the mutationSignatures Class.

Print method of the mutationSignatures Class.

Usage

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

## S4 method for signature 'mutationSignatures'
print(x)
```

Arguments

object	the mutationSignatures object being shown
x	the mutationSignatures object being printed

---

show,mutFrameworkParams-method

Show method of the mutFrameworkParams Class.

Description

Show method of the mutFrameworkParams Class.

Print method of the mutFrameworkParams Class.

Usage

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

## S4 method for signature 'mutFrameworkParams'
print(x)
```

Arguments

object	the mutFrameworkParams object being shown
x	the mutFrameworkParams object being printed

---

show,mutSignExposures-method *Show method of the mutSignExposures Class.*

Description

Show method of the mutSignExposures Class.

Print method of the mutSignExposures Class.

Usage

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

## S4 method for signature 'mutSignExposures'
print(x)
```

Arguments

object	the mutSignExposures object being shown
x	the mutSignExposures object being printed

---

silhouetteMLB *Silhouette Analysis.*

Description

Analyze the clustering quality and generate a Silhouette Plot.

Usage

```
silhouetteMLB(data, fac, method = "cosine", plot = TRUE)
```

Arguments

data	numeric matrix
fac	clustering factor
method	method to be used as distance function. Defaults to c("cosine")
plot	logical, shall a barplot showing the cluster silhouettes be printed

Value

numeric vector including the silhouette values of the data poointts in the input matrix

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6
4. **Silhouette analysis in R**: http://www.biotechworld.it/bioinf/2017/01/20/translating-matlabs-silhouett

Examples

```
library(mutSignatures)
x <- mutSignatures:::getTestRunArgs("silhouetteMLB")
y <- silhouetteMLB(data = x$data, fac = x$fac)
y
```

---

simplifySignatures *Simplify Mutational Signatures.*

Description

This function is useufl when working with non-standard muation types, such as tetra-nnucleotide mutation types or mutation types with long/complex context. THe goal of this function is to aggregated together mutations that can be simplified because of a common mutation core. For example, mutation types AA[A>T]A, TA[A>T]A, CA[A>T]A, and GA[A>T]A can be simplified to the core tri-nucleotide mutation A[A>T]A. THis function identifies mergeable mutation types, and aggregates the corresponding counts/freqs.

Usage

```
simplifySignatures(x, asMutationSignatures = TRUE)
```

Arguments

x	a mutationSignatures-class object
asMutationSignatures	logical, shall the results be returned as a mutationSignatures-class object

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

object including simplified mutational signatures data

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- data.frame(Sig1=1:5, Sig2=5:1, Sig3=1:5)
A <- A/apply(A, 2, sum)
rownames(A) <- c("AA[C>A]A", "CA[C>A]A", "TA[C>A]A", "TA[C>G]A", "A[C>G]AT")
A <- mutSignatures::as.mutation.signatures(A)
mutSignatures::simplifySignatures(x = A)
```

---

sortByMutations *Sort Data by Mutation Type.*

Description

Reorder a mutationSignatures, mutationCounts, data.frame, or matrix object by sorting entries by mutation type.

Usage

```
sortByMutations(x)
```

Arguments

x	an object storing mutation count data

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

an object of the same class as x, with entries sorted according to mutation types.

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **Official website**: http://www.mutsignatures.org
2. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
3. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- data.frame(S1=1:5, S2=5:1, S3=1:5)
rownames(A) <- c("A[A>T]G", "A[C>G]G", "T[A>T]G", "T[C>G]T", "T[C>G]G")
mutSignatures::sortByMutations(A)
```

---

table2df *Table Mutation Types by Sample.*

Description

Prepare a molten data.frame starting from a mutation count matrix. Mutation types (rows) are countes for each sample (cols). The results are returned in a 3-column data.frame.

Usage

```
table2df(dataMatrix, rowLab = "sample", colLab = "feature", valueLab = "count")
```

Arguments

dataMatrix	a numeric matrix including mutation counts
rowLab	string, name for the column that will be storing row IDs, typically sample IDs
colLab	string, name for the column that will be storing column IDs, typically sample IDs
valueLab	string, name for the column that will be storing mutation count values

Details

This function is part of the user-interface set of tools included in mutSignatures. This is an exported function.

Value

data.frame storing mutation counts by sample

Author(s)

Damiano Fantini, <damiano.fantini@gmail.com>

References

More information and examples about mutational signature analysis can be found here:

1. **More info and examples** about the mutSignatures R library: https://www.data-pulse.com/dev_site/mutsignatures/
2. **Oncogene paper**, Mutational Signatures Operative in Bladder Cancer: https://www.nature.com/articles/s41388-017-0099-6

Examples

```
A <- cbind(`A>G`=c(5,10),`A>T`=c(3,20),`A>C`=c(15,0))
rownames(A) = c("Smpl1", "Smpl2")
mutSignatures::table2df(A)
```

[,mutationCounts,numeric,ANY,ANY-method

Subset a mutationCounts-class object.

Description

Subset a mutationCounts-class object.

Usage

```
## S4 method for signature 'mutationCounts,numeric,ANY,ANY'
x[i]
```

Arguments

x	a mutationCounts-class object to subset
i	numeric, indeces of the elements to be extracted

[,mutationSignatures,numeric,ANY,ANY-method

Subset a mutationSignatures-class object.

Description

Subset a mutationSignatures-class object.

Usage

```
## S4 method for signature 'mutationSignatures,numeric,ANY,ANY'
x[i]
```

Arguments

x	a mutationSignatures-class object to subset
i	numeric, indeces of the elements to be extracted

[,mutSignExposures,numeric,ANY,ANY-method

Subset a mutSignExposures-class object.

Description

Subset a mutSignExposures-class object.

Usage

```
## S4 method for signature 'mutSignExposures,numeric,ANY,ANY'
x[i]
```

Arguments

x	a mutSignExposures-class object to subset
i	numeric, indeces of the elements to be extracted

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