

Package ‘RESOLVE’

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Title RESOLVE: An R package for the efficient analysis of mutational signatures from cancer genomes

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Suggests BiocGenerics, BiocStyle, testthat, knitr

Description Cancer is a genetic disease caused by somatic mutations in genes controlling key biological functions such as cellular growth and division. Such mutations may arise both through cell-intrinsic and exogenous processes, generating characteristic mutational patterns over the genome named mutational signatures. The study of mutational signatures have become a standard component of modern genomics studies, since it can reveal which (environmental and endogenous) mutagenic processes are active in a tumor, and may highlight markers for therapeutic response. Mutational signatures computational analysis presents many pitfalls. First, the task of determining the number of signatures is very complex and depends on heuristics. Second, several signatures have no clear etiology, casting doubt on them being computational artifacts rather than due to mutagenic processes. Last, approaches for signatures assignment are greatly influenced by the set of signatures used for the analysis. To overcome these limitations, we developed RESOLVE (Robust ESTimation Of mutational signatures Via rEgularization), a framework that allows the efficient extraction and assignment of mutational signatures. RESOLVE implements a novel algorithm that enables (i) the efficient extraction, (ii) exposure estimation, and (iii) confidence assessment during the computational inference of mutational signatures.

Encoding UTF-8

License file LICENSE

URL <https://github.com/danro9685/RESOLVE>

BugReports <https://github.com/danro9685/RESOLVE/issues>

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RESOLVE-package	<i>An R package for the efficient analysis of mutational signatures from cancer genomes.</i>
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Description

This package provides a framework that allows for the efficient extraction and assignment of mutational signatures. It implements a novel algorithm that enables: (i) the efficient extraction, (ii) exposure estimation, and (iii) confidence assessment during the computational inference of mutational signatures. RESOLVE performs de novo signatures extraction by regularized Non-Negative Matrix Factorization. The method incorporates a background signature during the inference step and adopts elastic net regression with LASSO penalty to reduce the impact of overfitting. The estimation of the optimal number of signatures is performed by bi-cross-validation.

background	<i>Germline replication error</i>
------------	-----------------------------------

Description

Germline replication error estimated in Rahbari, Raheleh, et al. (2016).

Usage

```
data(background)
```

Format

Vector of rates

Value

Vector of rates for the 96 trinucleotides

Source

Nat Genet. 2016 Feb;48(2):126-133 (<https://www.nature.com/articles/ng.3469>).

background2	<i>COSMIC replication error</i>
-------------	---------------------------------

Description

Background replication error signature derived from COSMIC SBS5.

Usage

```
data(background2)
```

Format

Vector of rates

Value

Vector of rates for the 96 trinucleotides

Source

COSMIC database (<https://cancer.sanger.ac.uk/cosmic/signatures>) v3.

cn_example_reduced	<i>A reduced version of the copy number data for 5 TCGA samples in the format compatible with the import function</i>
--------------------	---

Description

Reduced version of the dataset of counts of copy numbers detected in TCGA tumors published in Steele, Christopher D., et al. (2022).

Usage

```
data(cn_example_reduced)
```

Format

Reduced version of the counts of copy numbers in the format compatible with the import function

Value

Reduced version of the counts of copy numbers for 5 tumors and 48 copy number classes in the format compatible with the import function

Source

Nature. 2022 Jun;606(7916):984-991 (<https://www.nature.com/articles/s41586-022-04738-6>).

getCNCOUNTS	<i>getCNCOUNTS</i>
-------------	--------------------

Description

Create Copy Numbers (CNs) counts matrix from input data. This function has been derived from: https://github.com/UCL-Research-Department-of-Pathology/panConusig/blob/main/R/setup_CNsig.R

Usage

```
getCNCOUNTS(data)
```

Arguments

data	A data.frame with copy number data having 6 columns: sample name, chromosome, start position, end position, major CN, minor CN.
------	---

Value

A matrix with Copy Numbers (CNs) counts per patient.

Examples

```
data(cn_example_reduced)
res <- getCNCOUNTS(data = cn_example_reduced)
```

getIDCOUNTS	<i>getIDCOUNTS</i>
-------------	--------------------

Description

Create Small Insertions and Deletions (IDs) counts matrix from input data.

Usage

```
getIDCOUNTS(data, reference = NULL)
```

Arguments

data	A data.frame with variants having 6 columns: sample name, chromosome, start position, end position, ref, alt.
reference	A BSgenome object with the reference genome to be used.

Value

A matrix with Small Insertions and Deletions (IDs) counts per patient.

Examples

```
library('BSgenome.Hsapiens.1000genomes.hs37d5')
data(id_example_reduced)
res <- getIDCounts(data = id_example_reduced, reference = BSgenome.Hsapiens.1000genomes.hs37d5)
```

getMNVCounts	<i>getMNVCounts</i>
--------------	---------------------

Description

Create Multi-Nucleotide Variants (MNVs) counts matrix from input data.

Usage

```
getMNVCounts(data)
```

Arguments

data	A data.frame with variants having 6 columns: sample name, chromosome, start position, end position, ref, alt.
------	---

Value

A matrix with Multi-Nucleotide Variants (MNVs) counts per patient.

Examples

```
data(ssm560_reduced)
res <- getMNVCounts(data = ssm560_reduced)
```

getSBSCounts	<i>getSBSCounts</i>
--------------	---------------------

Description

Create Single Base Substitutions (SBS) counts matrix from input data for a provided reference genome.

Usage

```
getSBSCounts(data, reference = NULL)
```

Arguments

data	A data.frame with variants having 6 columns: sample name, chromosome, start position, end position, ref, alt.
reference	A BSgenome object with the reference genome to be used to retrieve flanking bases.

Value

A matrix with Single Base Substitutions (SBS) counts per patient.

Examples

```
library('BSgenome.Hsapiens.1000genomes.hs37d5')
data(ssm560_reduced)
res <- getSBSCounts(data = ssm560_reduced, reference = BSgenome.Hsapiens.1000genomes.hs37d5)
```

groupsCNPlot	<i>groupsCNPlot</i>
--------------	---------------------

Description

Plot observed Copy Number (CN) counts for different groups of patients.

Usage

```
groupsCNPlot(counts, groups, normalize = TRUE, xlabel = FALSE)
```

Arguments

counts	Matrix with Copy Number (CN) counts data.
groups	List where names are groups labels and elements are patients labels corresponding to rownames in counts.
normalize	Boolean value; shall I normalize observed counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['groups.CN.plot']][['counts']]
groups <- plot_data_examples[['groups.CN.plot']][['groups']]
groupsCNPlot(counts=counts, groups=groups)
```

 groupsCXPlot

groupsCXPlot

Description

Plot observed Copy Number (Reduced, CX) counts for different groups of patients.

Usage

```
groupsCXPlot(counts, groups, normalize = TRUE, xlabels = FALSE)
```

Arguments

counts	Matrix with Copy Number (Reduced, CX) counts data.
groups	List where names are groups labels and elements are patients labels corresponding to rownames in counts.
normalize	Boolean value; shall I normalize observed counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['groups.CX.plot']][['counts']]
groups <- plot_data_examples[['groups.CX.plot']][['groups']]
groupsCXPlot(counts=counts, groups=groups)
```

 groupsIDPlot

groupsIDPlot

Description

Plot observed Small Insertions and Deletions (ID) counts for different groups of patients.

Usage

```
groupsIDPlot(counts, groups, normalize = TRUE, xlabels = FALSE)
```


Arguments

counts	Matrix with Small Insertions and Deletions (ID) counts data.
groups	List where names are groups labels and elements are patients labels corresponding to rownames in counts.
normalize	Boolean value; shall I normalize observed counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['groups.ID.plot']][['counts']]
groups <- plot_data_examples[['groups.ID.plot']][['groups']]
groupsIDPlot(counts=counts, groups=groups)
```

groupsMNVPlot

groupsMNVPlot

Description

Plot observed Multi-Nucleotide Variants (MNVs) counts for different groups of patients.

Usage

```
groupsMNVPlot(counts, groups, normalize = TRUE, xlabels = FALSE)
```

Arguments

counts	Matrix with Multi-Nucleotide Variants (MNVs) counts data.
groups	List where names are groups labels and elements are patients labels corresponding to rownames in counts.
normalize	Boolean value; shall I normalize observed counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['groups.MNV.plot']][['counts']]
groups <- plot_data_examples[['groups.MNV.plot']][['groups']]
groupsMNVPlot(counts=counts, groups=groups)
```

groupsSBSPlot	<i>groupsSBSPlot</i>
---------------	----------------------

Description

Plot observed Single Base Substitutions (SBS) counts for different groups of patients.

Usage

```
groupsSBSPlot(counts, groups, normalize = TRUE, xlabels = FALSE)
```

Arguments

counts	Matrix with Single Base Substitutions (SBS) counts data.
groups	List where names are groups labels and elements are patients labels corresponding to rownames in counts.
normalize	Boolean value; shall I normalize observed counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['groups.SBS.plot']][['counts']]
groups <- plot_data_examples[['groups.SBS.plot']][['groups']]
groupsSBSPlot(counts=counts,groups=groups)
```

id_example_reduced	<i>A reduced version of the indel data for 3 samples in the format compatible with the import function</i>
--------------------	--

Description

Reduced version of the dataset of counts of indels detected in 3 samples from Osorio, Fernando G., et al. (2018).

Usage

```
data(id_example_reduced)
```

Format

Reduced version of the counts of indels in the format compatible with the import function

Value

Reduced version of the counts of indels for 3 samples and 83 indel classes in the format compatible with the import function

Source

Cell Rep. 2018 Nov 27;25(9):2308-2316.e4 (10.1016/j.celrep.2018.11.014).

patients

Point mutations for 560 breast tumors

Description

Dataset of counts of the point mutations detected in 560 breast tumors published in Nik-Zainal, Serena, et al. (2016).

Usage

data(patients)

Format

Counts of the point mutations

Value

Counts of point mutations for 560 tumors and 96 trinucleotides

Source

Nature. 2016 Jun 2;534(7605):47-54 (<https://www.nature.com/articles/nature17676>).

patientsCNPlot *patientsCNPlot*

Description

Plot Copy Number (CN) counts for a set of given patients.

Usage

```
patientsCNPlot(  
  cn_data_counts,  
  samples = rownames(cn_data_counts),  
  freq = FALSE,  
  xlabel = FALSE  
)
```

Arguments

`cn_data_counts` Copy Number counts matrix.
`samples` Name of the samples. This should match a rownames in `cn_data_counts`
`freq` Boolean value; shall I display rates instead of counts?
`xlabels` Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)  
counts <- plot_data_examples[['patients.CN.plot']][['counts']]  
patientsCNPlot(cn_data_counts=counts, samples=rownames(counts)[seq_len(2)])
```

patientsCXPlot *patientsCXPlot*

Description

Plot Copy Number (Reduced, CX) counts for a set of given patients.

Usage

```
patientsCXPlot(
  cn_data_counts,
  samples = rownames(cn_data_counts),
  freq = FALSE,
  xlabel = FALSE
)
```

Arguments

cn_data_counts Copy Number counts matrix.
 samples Name of the samples. This should match a rownames in cn_data_counts
 freq Boolean value; shall I display rates instead of counts?
 xlabel Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['patients.CX.plot']][['counts']]
patientsCXPlot(cn_data_counts=counts, samples=rownames(counts)[seq_len(2)])
```

patientsIDPlot *patientsIDPlot*

Description

Plot Small Insertions and Deletions (ID) counts for a set of given patients.

Usage

```
patientsIDPlot(
  id_data_counts,
  samples = rownames(id_data_counts),
  freq = FALSE,
  xlabel = FALSE
)
```

Arguments

id_data_counts Small Insertions and Deletions counts matrix.
 samples Name of the samples. This should match a rownames in id_data_counts
 freq Boolean value; shall I display rates instead of counts?
 xlabel Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['patients.ID.plot']][['counts']]
patientsIDPlot(id_data_counts=counts, samples=rownames(counts)[seq_len(2)])
```

patientsMNVPlot *patientsMNVPlot*

Description

Plot Multi-Nucleotide Variants (MNVs) counts for a set of given patients.

Usage

```
patientsMNVPlot(
  multi_nucleotides_counts,
  samples = rownames(multi_nucleotides_counts),
  freq = FALSE,
  xlabel = FALSE
)
```

Arguments

multi_nucleotides_counts	Multi-Nucleotide counts matrix.
samples	Name of the samples. This should match a rownames in multi_nucleotides_counts
freq	Boolean value; shall I display rates instead of counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
counts <- plot_data_examples[['patients.MNV.plot']][['counts']]
patientsMNVPlot(multi_nucleotides_counts=counts, samples=rownames(counts)[seq_len(2)])
```

patientsSBSPlot *patientsSBSPlot*

Description

Plot Single Base Substitutions (SBS) counts for a set of given patients.

Usage

```
patientsSBSPlot(  
  trinucleotides_counts,  
  samples = rownames(trinucleotides_counts),  
  freq = FALSE,  
  xlabels = FALSE  
)
```

Arguments

trinucleotides_counts	Trinucleotides counts matrix.
samples	Name of the samples. This should match a rownames in trinucleotides_counts.
freq	Boolean value; shall I display rates instead of counts?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)  
counts <- plot_data_examples[['patients.SBS.plot']] [['counts']]  
patientsSBSPlot(trinucleotides_counts=counts, samples=rownames(counts)[seq_len(2)])
```

plot_data_examples *List data structure to run examples*

Description

List data structure to run examples.

Usage

```
data(plot_data_examples)
```

Format

List data structure to run examples

Value

List data structure to run examples

Source

List data structure to run examples.

signaturesAssignment *signaturesAssignment*

Description

Perform the assignment of K somatic mutational signatures provided as input to samples given a set of observed counts x . This function can be used to estimate different types of mutational signatures such as: SBS (single base substitutions) and MNV (multi-nucleotide variant) (see Degasper, Andrea, et al. 'Substitution mutational signatures in whole-genome-sequenced cancers in the UK population.' *Science* 376.6591 (2022): ab19283), CX (chromosomal instability) (see Drews, Ruben M., et al. 'A pan-cancer compendium of chromosomal instability.' *Nature* 606.7916 (2022): 976-983) and CN (copy number) signatures (see Steele, Christopher D., et al. 'Signatures of copy number alterations in human cancer.' *Nature* 606.7916 (2022): 984-991).

Usage

```
signaturesAssignment(x, beta)
```

Arguments

<code>x</code>	Counts matrix for a set of n patients and m categories. These can be, e.g., SBS, MNV, CN or CN counts; in the case of SBS it would be an n patients \times 96 trinucleotides matrix.
<code>beta</code>	Matrix of the discovered signatures to be used for the assignment.

Value

A list with the discovered signatures. It includes 3 elements: `alpha`: matrix of the discovered exposure values. `beta`: matrix of the discovered signatures. `unexplained_mutations`: number of unexplained mutations per sample.

Examples

```
data(background)
data(patients)
set.seed(12345)
beta <- signaturesDecomposition(x = patients[seq_len(3),seq_len(2)],
                              K = 3,
                              background_signature = background[seq_len(2)],
                              nmf_runs = 2,
                              num_processes = 1)

set.seed(12345)
res <- signaturesAssignment(x = patients[seq_len(3),seq_len(2)], beta = beta$beta[[1]])
```

signaturesCNPlot	<i>signaturesCNPlot</i>
------------------	-------------------------

Description

Plot the inferred Copy Number (CN) mutational signatures.

Usage

```
signaturesCNPlot(beta, useRowNames = FALSE, xlabels = FALSE)
```

Arguments

beta	Matrix with the inferred mutational signatures.
useRowNames	Boolean value; shall I use the rownames from beta as names for the signatures?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
beta <- plot_data_examples[['signatures.CN.plot']][['beta']]
signaturesCNPlot(beta=beta)
```

 signaturesCV

signaturesCV

Description

Perform the assessment of different signaturesDecomposition solutions by cross-validation for K (beta, as estimated by signaturesDecomposition) somatic mutational signatures given a set of observations x and discovered signatures beta.

Usage

```
signaturesCV(
  x,
  beta,
  normalize_counts = FALSE,
  cross_validation_entries = 0.01,
  cross_validation_iterations = 5,
  cross_validation_repetitions = 100,
  num_processes = Inf,
  verbose = TRUE
)
```

Arguments

x	Counts matrix for a set of n patients and m categories. These can be, e.g., SBS, MNV, CN or CN counts; in the case of SBS it would be an n patients x 96 trinucleotides matrix.
beta	A set of inferred signatures as returned by signaturesDecomposition function.
normalize_counts	If true, the input counts matrix x is normalized such that the patients have the same number of mutation.
cross_validation_entries	Percentage of cells in the counts matrix to be replaced by 0s during cross-validation.
cross_validation_iterations	For each configuration, the first time the signatures are fitted form a matrix with a percentage of values replaced by 0s. This may result in poor fit/results. Then, we perform predictions of these entries and replace them with such predicted values. This parameter is the number of restarts to be performed to improve this estimate and obtain more stable solutions.
cross_validation_repetitions	Number of time cross-validation should be repeated. Higher values result in better estimate, but are computationally more expensive.
num_processes	Number of processes to be used during parallel execution. To execute in single process mode, this parameter needs to be set to either NA or NULL.
verbose	Boolean. Shall I print information messages?

Value

A list of 2 elements: estimates and summary. Here, `cv_estimates` reports the mean squared error for each configuration of performed cross-validation; `rank_estimates` reports mean and median values for each value of `K`.

Examples

```
data(background)
data(patients)
set.seed(12345)
sigs <- signaturesDecomposition(x = patients[seq_len(3),seq_len(2)],
                              K = 3:4,
                              background_signature = background[seq_len(2)],
                              nmf_runs = 2,
                              num_processes = 1)

set.seed(12345)
res <- signaturesCV(x = patients[seq_len(3),seq_len(2)],
                   beta = sigs$beta,
                   cross_validation_iterations = 2,
                   cross_validation_repetitions = 2,
                   num_processes = 1)
```

 signaturesCXPlot

signaturesCXPlot

Description

Plot the inferred Copy Number (Reduced, CX) mutational signatures.

Usage

```
signaturesCXPlot(beta, useRowNames = FALSE, xlabels = FALSE)
```

Arguments

<code>beta</code>	Matrix with the inferred mutational signatures.
<code>useRowNames</code>	Boolean value; shall I use the rownames from <code>beta</code> as names for the signatures?
<code>xlabels</code>	Boolean value; shall I display x labels?

Value

A `ggplot2` object.

Examples

```
data(plot_data_examples)
beta <- plot_data_examples[['signatures.CX.plot']][['beta']]
signaturesCXPlot(beta=beta)
```

 signaturesDecomposition

signaturesDecomposition

Description

Perform signatures discovery and rank estimation for a range of K somatic mutational signatures given a set of observed counts x . This function can be used to estimate different types of mutational signatures such as: SBS (single base substitutions) and MNV (multi-nucleotide variant) (see Degasperi, Andrea, et al. 'Substitution mutational signatures in whole-genome-sequenced cancers in the UK population.' *Science* 376.6591 (2022): ab19283), CX (chromosomal instability) (see Drews, Ruben M., et al. 'A pan-cancer compendium of chromosomal instability.' *Nature* 606.7916 (2022): 976-983) and CN (copy number) signatures (see Steele, Christopher D., et al. 'Signatures of copy number alterations in human cancer.' *Nature* 606.7916 (2022): 984-991).

Usage

```
signaturesDecomposition(
  x,
  K,
  background_signature = NULL,
  normalize_counts = FALSE,
  nmf_runs = 100,
  num_processes = Inf,
  verbose = TRUE
)
```

Arguments

x	Counts matrix for a set of n patients and m categories. These can be, e.g., SBS, MNV, CN or CN counts; in the case of SBS it would be an n patients \times 96 trinucleotides matrix.
K	Either one value or a range of numeric values (each of them greater than 0) indicating the number of signatures to be considered.
<code>background_signature</code>	Background signature to be used.
<code>normalize_counts</code>	If true, the input counts matrix x is normalized such that the patients have the same number of mutation.
<code>nmf_runs</code>	Number of iteration (minimum 1) of NMF to be performed for a robust estimation of beta.
<code>num_processes</code>	Number of processes to be used during parallel execution. To execute in single process mode, this parameter needs to be set to either NA or NULL.
<code>verbose</code>	Boolean. Shall I print information messages?

Value

A list with the discovered signatures and related rank measures. It includes 5 elements: alpha: list of matrices of the discovered exposure values for each possible rank in the range K. beta: list of matrices of the discovered signatures for each possible rank in the range K. unexplained_mutations: number of unexplained mutations per sample. cosine_similarity: cosine similarity comparing input data x and predictions for each rank in the range K. measures: a data.frame containing the quality measures for each possible rank in the range K.

Examples

```
data(background)
data(patients)
set.seed(12345)
res <- signaturesDecomposition(x = patients[seq_len(3),seq_len(2)],
                             K = 3:4,
                             background_signature = background[seq_len(2)],
                             nmf_runs = 2,
                             num_processes = 1)
```

signaturesIDPlot *signaturesIDPlot*

Description

Plot the inferred Small Insertions and Deletions (ID) mutational signatures.

Usage

```
signaturesIDPlot(beta, useRowNames = FALSE, xlabels = FALSE)
```

Arguments

beta	Matrix with the inferred mutational signatures.
useRowNames	Boolean value; shall I use the rownames from beta as names for the signatures?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
beta <- plot_data_examples[['signatures.ID.plot']][['beta']]
signaturesIDPlot(beta=beta)
```

signaturesMNVPlot *signaturesMNVPlot*

Description

Plot the inferred Multi-Nucleotide Variants (MNVs) mutational signatures.

Usage

```
signaturesMNVPlot(beta, useRowNames = FALSE, xlabels = FALSE)
```

Arguments

beta	Matrix with the inferred mutational signatures.
useRowNames	Boolean value; shall I use the rownames from beta as names for the signatures?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
beta <- plot_data_examples[['signatures.MNV.plot']][['beta']]
signaturesMNVPlot(beta=beta)
```

signaturesSBSPlot *signaturesSBSPlot*

Description

Plot the inferred Single Base Substitutions (SBS) mutational signatures.

Usage

```
signaturesSBSPlot(beta, useRowNames = FALSE, xlabels = FALSE)
```

Arguments

beta	Matrix with the inferred mutational signatures.
useRowNames	Boolean value; shall I use the rownames from beta as names for the signatures?
xlabels	Boolean value; shall I display x labels?

Value

A ggplot2 object.

Examples

```
data(plot_data_examples)
beta <- plot_data_examples[['signatures.SBS.plot']][['beta']]
signaturesSBSPlot(beta=beta)
```

signaturesSignificance

signaturesSignificance

Description

Perform a robust estimation of alpha coefficients by bootstrap to reach a certain level of cosine similarity given a set of observed counts *x* and discovered signatures *beta*.

Usage

```
signaturesSignificance(
  x,
  beta,
  cosine_thr = 0.95,
  min_contribution = 0.05,
  pvalue_thr = 0.05,
  nboot = 100,
  num_processes = Inf,
  verbose = TRUE
)
```

Arguments

<i>x</i>	Counts matrix for a set of <i>n</i> patients and <i>m</i> categories. These can be, e.g., SBS, MNV, CN or CN counts; in the case of SBS it would be an <i>n</i> patients x 96 trinucleotides matrix.
<i>beta</i>	Discovered signatures to be used for the fit of alpha.
<i>cosine_thr</i>	Level of cosine similarity to be reached for the fit of alpha.
<i>min_contribution</i>	Minimum contribution of a signature to be considered significant.
<i>pvalue_thr</i>	Pvalue level to be used to assess significance.
<i>nboot</i>	Number of bootstrap iterations to be performed.
<i>num_processes</i>	Number of processes to be used during parallel execution. To execute in single process mode, this parameter needs to be set to either NA or NULL.
<i>verbose</i>	Boolean. Shall I print information messages?

Value

A list with the bootstrap estimates. It includes 5 elements: alpha: matrix of the discovered exposure values considering significant signatures as estimated by bootstrap. beta: matrix of the discovered signatures. unexplained_mutations: number of unexplained mutations per sample. goodness_fit: vector reporting cosine similarities between predictions and observations. bootstrap_estimates: list of matrices reporting results by bootstrap estimates.

Examples

```
data(background)
data(patients)
set.seed(12345)
beta <- signaturesDecomposition(x = patients[seq_len(3),seq_len(2)],
                              K = 3:4,
                              background_signature = background[seq_len(2)],
                              nmf_runs = 2,
                              num_processes = 1)

set.seed(12345)
res <- signaturesSignificance(x = patients[seq_len(3),seq_len(2)],
                             beta = beta$beta[[1]],
                             cosine_thr = 0.95,
                             min_contribution = 0.05,
                             pvalue_thr = 0.05,
                             nboot = 5,
                             num_processes = 1)
```

ssm560_reduced	<i>A reduced version of the point mutations for 560 breast tumors in the format compatible with the import function</i>
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Description

Reduced version of the dataset of counts of the point mutations detected in 560 breast tumors published in Nik-Zainal, Serena, et al. (2016).

Usage

```
data(ssm560_reduced)
```

Format

Reduced version of the counts of the point mutations in the format compatible with the import function

Value

Reduced version of the counts of point mutations for 560 tumors and 96 trinucleotides in the format compatible with the import function

Source

Nature. 2016 Jun 2;534(7605):47-54 (<https://www.nature.com/articles/nature17676>).

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