Package 'SparseSignatures'

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Title SparseSignatures

Depends R (>= 4.1.0), NMF

Imports nnlasso, nnls, parallel, data.table, Biostrings,
GenomicRanges, IRanges, BSgenome, GenomeInfoDb, ggplot2,
gridExtra, reshape2, RhpcBLASctl

Suggests BiocGenerics, BSgenome.Hsapiens.1000genomes.hs37d5,
BiocStyle, testthat, knitr,

Name An R package for the extraction of sparse mutational signatures
from whole genome sequencing data

Description
Point mutations occurring in a genome can be divided into 96 categories based on the base be-
ing mutated, the base it is mutated into and its two flanking bases. Therefore, for any pa-
tient, it is possible to represent all the point mutations occurring in that patient's tumor as a vec-
tor of length 96, where each element represents the count of mutations for a given cate-
gory in the patient. A mutational signature represents the pattern of mutations produced by a mu-
tagen or mutagenic process inside the cell. Each signature can also be represented by a vec-
tor of length 96, where each element represents the probability that this particular mutagenic pro-
cess generates a mutation of the 96 above mentioned categories. In this R package, we pro-
vide a set of functions to extract and visualize the mutational signatures that best explain the mu-
tation counts of a large number of patients.

Encoding UTF-8

License file LICENSE

URL https://github.com/danro9685/SparseSignatures

BugReports https://github.com/danro9685/SparseSignatures

biocViews BiomedicalInformatics, SomaticMutation

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Contents

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background	*germline replication error*

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

Rahbari, Raheleh, et al. "Timing, rates and spectra of human germline mutation." Nature genetics 48.2 (2016): 126.

---

background2	*COSMIC replication error*

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.

cv_example	*example of results obtained with the function nmf.LassoCV on the counts input from Nik-Zainal, Serena, et al. (2016).*

Description

example of results obtained with the function nmf.LassoCV on the counts input from Nik-Zainal, Serena, et al. (2016).

Usage

```
data(cv_example)
```

Format

results obtained with the function nmf.LassoCV on the counts input from Nik-Zainal, Serena, et al. (2016)

Value

results obtained with the function nmf.LassoCV on the counts input from Nik-Zainal, Serena, et al. (2016)

---

import.trinucleotides.counts

import.trinucleotides.counts

Description

Make trinucleotides counts matrix from input data for a given reference genome.

Usage

```
import.trinucleotides.counts(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 trinucleotides counts per patient.

Examples

```
data(ssm560_reduced)
library("BSgenome.Hsapiens.1000genomes.hs37d5")
trinucleotides_counts = import.trinucleotides.counts(data=ssm560_reduced,
    reference=BSgenome.Hsapiens.1000genomes.hs37d5)
```

---

imported_data	*example of imported data from Nik-Zainal, Serena, et al. (2016).*

Description

example of imported data from Nik-Zainal, Serena, et al. (2016).

Usage

```
data(imported_data)
```

Format

results obtained with the function import.counts.data on the data from Nik-Zainal, Serena, et al. (2016)

Value

results obtained with the function import.counts.data on the data from Nik-Zainal, Serena, et al. (2016)

---

lambdaRangeAlphaEvaluation	
	lambdaRangeAlphaEvaluation

Description

Estimate the range of lambda values for alpha to be considered in the signature inference. Note that too small values of lambda result in dense exposures, but too large values lead to bad fit of the counts.

Usage

```
lambdaRangeAlphaEvaluation(
  x,
  K = 5,
  beta = NULL,
  background_signature = NULL,
  normalize_counts = TRUE,
  nmf_runs = 10,
  lambda_values = c(0.01, 0.05, 0.1, 0.2),
  iterations = 30,
  max_iterations_lasso = 10000,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
  log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
K	numeric value (minimum 2) indicating the number of signatures to be discovered.
beta	starting beta for the estimation. If it is NULL, starting beta is estimated by NMF.
background_signature	
	background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.
normalize_counts	
	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.
lambda_values	value of LASSO to be used for alpha between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_values is, the sparser are the resulting exposures, but too large values may result in a reduced fit of the observed counts.
iterations	Number of iterations to be performed. Each iteration corresponds to a first step where beta is fitted and a second step where alpha is fitted.
max_iterations_lasso	
	Number of maximum iterations to be performed during the sparsification via Lasso.
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.
seed	Seed for reproducibility.
verbose	boolean; Shall I print all messages?

log_file   log file where to print outputs when using parallel. If parallel execution is dis-
                 abled, this parameter is ignored.

Value

A list corresponding to results of the function nmfLasso for each value of lambda to be tested. This
function allows to test a good range of lambda values for alpha to be considered. One should keep
in mind that too small values generate dense solution, while too high ones leads to poor fit. This
behavior is resampled in the values of loglik_progression, which should be increasing: too small
values of lambda results in unstable log-likelihood through the iterations, while too large values
make log-likelihood drop.

Examples

```
data(background)
data(patients)
res = lambdaRangeAlphaEvaluation(x=patients[1:100,],
    K=5,background_signature=background,
    nmf_runs=1,lambda_values=c(0.01,0.05),
    num_processes=NA,
    seed=12345)
```

---

lambdaRangeBetaEvaluation

lambdaRangeBetaEvaluation

Description

Estimate the range of lambda values for beta to be considered in the signature inference. Note that
too small values of lambda result in dense signatures, but too large values lead to bad fit of the
counts.

Usage

```
lambdaRangeBetaEvaluation(
  x,
  K = 5,
  beta = NULL,
  background_signature = NULL,
  normalize_counts = TRUE,
  nmf_runs = 10,
  lambda_values = c(0.01, 0.05, 0.1, 0.2),
  iterations = 30,
  max_iterations_lasso = 10000,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
```

```
    log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
K	numeric value (minimum 2) indicating the number of signatures to be discovered.
beta	starting beta for the estimation. If it is NULL, starting beta is estimated by NMF.
background_signature	background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.
normalize_counts	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.
lambda_values	value of LASSO to be used for beta between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_values is, the sparser are the resulting signatures, but too large values may result in a reduced fit of the observed counts.
iterations	Number of iterations to be performed. Each iteration corresponds to a first step where beta is fitted and a second step where alpha is fitted.
max_iterations_lasso	Number of maximum iterations to be performed during the sparsification via Lasso.
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.
seed	Seed for reproducibility.
verbose	boolean; Shall I print all messages?
log_file	log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list corresponding to results of the function nmfLasso for each value of lambda to be tested. This function allows to test a good range of lambda values for beta to be considered. One should keep in mind that too small values generate dense solution, while too high ones leads to poor fit. This behavior is resampled in the values of loglik_progression, which should be increasing: too small values of lambda results in unstable log-likelihood through the iterations, while too large values make log-likelihood drop.

Examples

```
data(background)
data(patients)
res = lambdaRangeBetaEvaluation(x=patients[1:100,],
     K=5,
     background_signature=background,
     nmf_runs=1,
     lambda_values=c(0.01,0.05),
     num_processes=NA,
     seed=12345)
```

---

lambda_range_example	*example of results obtained with the function evaluate.lambda.range on the counts input from Nik-Zainal, Serena, et al. (2016).*

Description

example of results obtained with the function evaluate.lambda.range on the counts input from Nik-Zainal, Serena, et al. (2016).

Usage

```
data(lambda_range_example)
```

Format

results obtained with the function evaluate.lambda.range on the counts input from Nik-Zainal, Serena, et al. (2016)

Value

results obtained with the function evaluate.lambda.range on the counts input from Nik-Zainal, Serena, et al. (2016)

---

mutation_categories	*trinucleotides mutation categories*

Description

96 trinucleotides mutation categories

Usage

```
data(mutation_categories)
```

Format

matrix of 96 trinucleotides mutation categories

Value

matrix of 96 trinucleotides mutation categories

---

nmfLasso   *nmfLasso*

Description

Perform the discovery of K somatic mutational signatures given a set of observed counts x.

Usage

```
nmfLasso(
  x,
  K,
  beta = NULL,
  background_signature = NULL,
  normalize_counts = TRUE,
  nmf_runs = 10,
  lambda_rate_alpha = 0.05,
  lambda_rate_beta = 0.05,
  iterations = 30,
  max_iterations_lasso = 10000,
  seed = NULL,
  verbose = TRUE
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
K	numeric value (minimum 2) indicating the number of signatures to be discovered.
beta	starting beta for the estimation. If it is NULL, starting beta is estimated by NMF.
background_signature	
	background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.
normalize_counts	
	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.

lambda_rate_alpha

value of LASSO to be used for alpha between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the exposure values to 0 within one step. The higher lambda_rate_alpha is, the sparser are the resulting exposure values, but too large values may result in a reduced fit of the observed counts.

lambda_rate_beta

value of LASSO to be used for beta between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_rate_beta is, the sparser are the resulting signatures, but too large values may result in a reduced fit of the observed counts.

iterations   Number of iterations to be performed. Each iteration corresponds to a first step where beta is fitted and a second step where alpha is fitted.

max_iterations_lasso

Number of maximum iterations to be performed during the sparsification via Lasso.

seed   Seed for reproducibility.

verbose   boolean; Shall I print all messages?

Value

A list with the discovered signatures. It includes 6 elements: alpha: matrix of the discovered exposure values beta: matrix of the discovered signatures starting_alpha: initial alpha on which the method has been applied starting_beta: initial beta on which the method has been applied log-lik_progression: log-likelihood values during the iterations. This values should be increasing, if not the selected value of lambda is too high best_loglik: log-likelihood of the best signatures configuration

Examples

```
data(patients)
data(starting_betas_example)
beta = starting_betas_example[["5_signatures","Value"]]
res = nmfLasso(x=patients[1:100,],
    K=5,
    beta=beta,
    lambda_rate_alpha=0.05,
    lambda_rate_beta=0.05,
    iterations=5,
    seed=12345)
```

nmfLassoBootstrap   *nmfLassoBootstrap*

Description

Perform the evaluation of different nmfLasso solutions by bootstrap for K (unknown) somatic mutational signatures given a set of observations x. The estimation can slow down because of memory usage and intensive computations, when a big number of bootstrap repetitions is asked and when the analysis is performed for a big range of signatures (K). In this case, an advice may be to split the computation into multiple smaller sets.

Usage

```
nmfLassoBootstrap(
  x,
  K = 3:10,
  starting_beta = NULL,
  background_signature = NULL,
  normalize_counts = TRUE,
  nmf_runs = 10,
  bootstrap_repetitions = 50,
  iterations = 30,
  max_iterations_lasso = 10000,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
  log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
K	a range of numeric value (each of them greater than 1) indicating the number of signatures to be discovered.
starting_beta	a list of starting beta value for each configuration of K. If it is NULL, starting betas are estimated by NMF.
background_signature	
	background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.
normalize_counts	
	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.
bootstrap_repetitions	
	Number of time bootstrap should be repeated. Higher values result in better estimate, but are computationally more expensive.
iterations	Number of iterations to be performed. Each iteration corresponds to a first step where beta is fitted and a second step where alpha is fitted.

max_iterations_lasso

Number of maximum iterations to be performed during the sparsification via Lasso.

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.

seed   Seed for reproducibility.

verbose   boolean; Shall I print all messages?

log_file   log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list of 3 elements: stability, RSS and evar. Here, stability reports the estimared cosine similarity for alpha and beta at each bootstrap repetition; RSS reports for each configuration the estimated residual sum of squares; finally, evar reports the explained variance.

Examples

```
data(background)
data(patients)
res = nmfLassoBootstrap(x=patients[1:100,],
    K=3:5,
    background_signature=background,
    nmf_runs=1,
    bootstrap_repetitions=2,
    num_processes=NA,
    seed=12345)
```

---

nmfLassoCV   *nmfLassoCV*

Description

Perform the assessment of different nmfLasso solutions by cross validation for K (unknown) somatic mutational signatures given a set of observations x. The estimation can slow down because of memory usage and intensive computations, when a big number of cross validation repetitions is asked and when the grid search is performed for a lot of configurations. In this case, an advice may be to split the computation into multiple smaller sets.

Usage

```
nmfLassoCV(
  x,
  K = 3:10,
  starting_beta = NULL,
  background_signature = NULL,
```

```
    normalize_counts = TRUE,
    nmf_runs = 10,
    lambda_values_alpha = c(0, 0.01, 0.05, 0.1),
    lambda_values_beta = c(0, 0.01, 0.05, 0.1),
    cross_validation_entries = 0.01,
    cross_validation_iterations = 5,
    cross_validation_repetitions = 50,
    iterations = 30,
    max_iterations_lasso = 10000,
    num_processes = Inf,
    seed = NULL,
    verbose = TRUE,
    log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
K	a range of numeric value (each of them greater than 1) indicating the number of signatures to be discovered.
starting_beta	a list of starting beta value for each configuration of K. If it is NULL, starting betas are estimated by NMF.
background_signature	
	background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.
normalize_counts	
	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.
lambda_values_alpha	
	value of LASSO to be used for alpha between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_rate_alpha is, the sparser are the resulting exposures, but too large values may result in a reduced fit of the observed counts.
lambda_values_beta	
	value of LASSO to be used for beta between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_rate_beta is, the sparser are the resulting exposures, but too large values may result in a reduced fit of the observed counts.
cross_validation_entries	
	Percentage of cells in the count matrix to be replaced by 0s during cross validation.
cross_validation_iterations	
	For each configuration, the first time the signatures are discovered 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.

iterations   Number of iterations to be performed. Each iteration corresponds to a first step where beta is fitted and a second step where alpha is fitted.

max_iterations_lasso

Number of maximum iterations to be performed during the sparsification via Lasso.

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.

seed   Seed for reproducibility.

verbose   boolean; Shall I print all messages?

log_file   log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list of 2 elements: grid_search_mse and and grid_search_loglik. Here, grid_search_mse reports the mean squared error for each configuration of performed cross validation; grid_search_loglik reports for each configuration the number of times the algorithm converged.

Examples

```
data(background)
data(patients)
res = nmfLassoCV(x=patients[1:100,],
    K=3:5,
    background_signature=background,
    nmf_runs=1,
    lambda_values_alpha=c(0.00),
    lambda_values_beta=c(0.00),
    cross_validation_repetitions=2,
    num_processes=NA,
    seed=12345)
```

---

nmf_LassoK_example   *example of results obtained with the function nmf.LassoK on the counts input from Nik-Zainal, Serena, et al. (2016).*

Description

example of results obtained with the function nmf.LassoK on the counts input from Nik-Zainal, Serena, et al. (2016).

Usage

```
data(nmf_LassoK_example)
```

Format

results obtained with the function nmf.LassoK on the counts input from Nik-Zainal, Serena, et al. (2016)

Value

results obtained with the function nmf.LassoK on the counts input from Nik-Zainal, Serena, et al. (2016)

---

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

Nik-Zainal, Serena, et al. "Landscape of somatic mutations in 560 breast cancer whole-genome sequences." Nature 534.7605 (2016): 47.

---

patients.plot	*patients.plot*

Description

Plot trinucleotides counts for a set of given patients.

Usage

```
patients.plot(
  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(patients)
patients.plot(trinucleotides_counts=patients,samples=c("PD10010a","PD10011a","PD10014a"))
```

---

sigAssignmentCV	*sigAssignmentCV*

Description

Perform the assessment of different sigAssignmentLasso solutions by cross validation for a given
set of somatic mutational signatures and observations x. The estimation can slow down because
of memory usage and intensive computations, when a big number of cross validation repetitions is
asked and when the grid search is performed for a lot of configurations. In this case, an advice may
be to split the computation into multiple smaller sets.

Usage

```
sigAssignmentCV(
  x,
  beta,
  normalize_counts = TRUE,
  lambda_values_alpha = c(0, 0.01, 0.05, 0.1),
  cross_validation_entries = 0.01,
  cross_validation_iterations = 5,
  cross_validation_repetitions = 50,
  max_iterations_lasso = 10000,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
  log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
beta	beta to be fixed during the estimation of alpha.
normalize_counts	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
lambda_values_alpha	value of LASSO to be used for alpha between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_rate_alpha is, the sparser are the resulting exposures, but too large values may result in a reduced fit of the observed counts.
cross_validation_entries	Percentage of cells in the count matrix to be replaced by 0s during cross validation.
cross_validation_iterations	For each configuration, the first time the signatures are discovered 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.
max_iterations_lasso	Number of maximum iterations to be performed during the sparsification via Lasso.
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.
seed	Seed for reproducibility.

verbose	boolean; Shall I print all messages?
log_file	log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list of 2 elements: grid_search_mse and and grid_search_loglik. Here, grid_search_mse reports the mean squared error for each configuration of performed cross validation; grid_search_loglik reports for each configuration the number of times the algorithm converged.

Examples

```
data(patients)
data(starting_betas_example)
beta = starting_betas_example[["5_signatures","Value"]]
res = sigAssignmentCV(x=patients[1:100,],
    beta=beta,
    lambda_values_alpha=c(0.00),
    cross_validation_repetitions=2,
    num_processes=NA,
    seed=12345)
```

---

sigAssignmentEvaluation

sigAssignmentEvaluation

Description

Estimate the range of lambda values for alpha to be considered in the signature assignment. Note that too small values of lambda result in dense exposures, but too large values lead to bad fit of the counts.

Usage

```
sigAssignmentEvaluation(
  x,
  beta,
  normalize_counts = TRUE,
  lambda_values = c(0.01, 0.05, 0.1, 0.2),
  max_iterations_lasso = 10000,
  num_processes = Inf,
  seed = NULL,
  verbose = TRUE,
  log_file = ""
)
```

Arguments

x	count matrix for a set of n patients and 96 trinucleotides.
beta	beta to be fixed during the estimation of alpha.
normalize_counts	
	if true, the input count matrix x is normalize such that the patients have the same number of mutation.
lambda_values	value of LASSO to be used for alpha between 0 and 1. This value should be greater than 0. 1 is the value of LASSO that would shrink all the signatures to 0 within one step. The higher lambda_values is, the sparser are the resulting exposures, but too large values may result in a reduced fit of the observed counts.
max_iterations_lasso	
	Number of maximum iterations to be performed during the sparsification via Lasso.
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.
seed	Seed for reproducibility.
verbose	boolean; Shall I print all messages?
log_file	log file where to print outputs when using parallel. If parallel execution is disabled, this parameter is ignored.

Value

A list corresponding to results of the function sigAssignmentLasso for each value of lambda to be tested. This function allows to test a good range of lambda values for alpha to be considered. One should keep in mind that too small values generate dense solution, while too high ones leads to poor fit. This behavior is resampled in the values of loglik_progression, which should be increasing: too small values of lambda results in unstable log-likelihood through the iterations, while too large values make log-likelihood drop.

Examples

```
data(patients)
data(starting_betas_example)
beta = starting_betas_example[["5_signatures","Value"]]
res = sigAssignmentEvaluation(x=patients[1:100,],
    beta=beta,
    lambda_values=c(0.01,0.05),
    num_processes=NA,
    seed=12345)
```

sigAssignmentLasso   *sigAssignmentLasso*

Description

Perform the assignment of somatic mutational signatures to patients given a set of observed counts x and signatures beta.

Usage

```
sigAssignmentLasso(
  x,
  beta,
  normalize_counts = TRUE,
  lambda_rate_alpha = 0.05,
  max_iterations_lasso = 10000,
  seed = NULL,
  verbose = TRUE
)
```

Arguments

x   count matrix for a set of n patients and 96 trinucleotides.

beta   beta to be fixed during the estimation of alpha.

normalize_counts
                   if true, the input count matrix x is normalize such that the patients have the same
                   number of mutation.

lambda_rate_alpha
                   value of LASSO to be used for alpha between 0 and 1. This value should be
                   greater than 0. 1 is the value of LASSO that would shrink all the exposure
                   values to 0 within one step. The higher lambda_rate_alpha is, the sparser are the
                   resulting exposure values, but too large values may result in a reduced fit of the
                   observed counts.

max_iterations_lasso
                   Number of maximum iterations to be performed during the sparsification via
                   Lasso.

seed   Seed for reproducibility.

verbose   boolean; Shall I print all messages?

Value

A list with the discovered signatures and their assignment to patients. It includes 2 elements: alpha: matrix of the assigned exposure values beta: matrix of the discovered signatures

Examples

```
data(patients)
data(starting_betas_example)
beta = starting_betas_example[["5_signatures","Value"]]
res = sigAssignmentLasso(x=patients[1:100,],beta=beta,lambda_rate_alpha=0.05,seed=12345)
```

---

signatures.plot   *signatures.plot*

Description

Plot the inferred mutational signatures.

Usage

```
signatures.plot(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(nmf_LassoK_example)
signatures.plot(beta=nmf_LassoK_example$beta)
```

---

ssm560_reduced   *a reduced version of the point mutations for 560 breast tumors in the*
                                  format compatible with the import function

---

Description

reduced versione 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 versione of the counts of the point mutations in the format compatible with the import function

Value

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

Source

Nik-Zainal, Serena, et al. "Landscape of somatic mutations in 560 breast cancer whole-genome sequences." Nature 534.7605 (2016): 47.

---

startingBetaEstimation

startingBetaEstimation

Description

Perform a robust estimation of the starting betas for the nmfLasso method

Usage

```
startingBetaEstimation(
  x,
  K = 3:10,
  background_signature = NULL,
  normalize_counts = TRUE,
  nmf_runs = 10,
  seed = NULL,
  verbose = TRUE
)
```

Arguments

x   count matrix for a set of n patients and 96 trinucleotides.

K   numeric value (minimum 2) indicating the number of signatures to be discovered.

background_signature

background signature to be used. If not provided, a warning is thrown and an initial value for it is estimated by NMF. If beta is not NULL, this parameter is ignored.

normalize_counts

if true, the input count matrix x is normalize such that the patients have the same number of mutation.

nmf_runs	number of iteration (minimum 1) of NMF to be performed for a robust estimation of starting beta. If beta is not NULL, this parameter is ignored.
seed	Seed for reproducibility.
verbose	boolean; Shall I print all messages?

Value

A list containing the starting beta values for each configuration of K.

Examples

```
data(background)
data(patients)
res = startingBetaEstimation(x=patients[1:100,],
    K=3:5,
    background_signature=background,
    nmf_runs=1,
    seed=12345)
```

---

starting_betas_example

example of results obtained with the function starting.betas.estimation on the counts input from Nik-Zainal, Serena, et al. (2016).

Description

example of results obtained with the function starting.betas.estimation on the counts input from Nik-Zainal, Serena, et al. (2016).

Usage

```
data(starting_betas_example)
```

Format

results obtained with the function starting.betas.estimation on the counts input from Nik-Zainal, Serena, et al. (2016)

Value

results obtained with the function starting.betas.estimation on the counts input from Nik-Zainal, Serena, et al. (2016)

Index