

Package ‘decompTumor2Sig’

April 15, 2020

Type Package

Title Decomposition of individual tumors into mutational signatures by signature refitting

Depends R(>= 3.6), ggplot2

Imports methods, Matrix, quadprog(>= 1.5-5), vcfR, GenomicRanges, stats, GenomicFeatures, Biostrings, BiocGenerics, S4Vectors, plyr, utils, graphics, BSgenome.Hsapiens.UCSC.hg19, TxDb.Hsapiens.UCSC.hg19.knownGene, VariantAnnotation, SummarizedExperiment, ggseqlogo, gridExtra, data.table

Suggests knitr, rmarkdown, BiocStyle

Version 2.2.0

Date 2019-08-18

Encoding UTF-8

Description Uses quadratic programming for signature refitting, i.e., to decompose the mutation catalog from an individual tumor sample into a set of given mutational signatures (either Alexandrov-model signatures or Shiraishi-model signatures), computing weights that reflect the contributions of the signatures to the mutation load of the tumor.

License GPL-2

URL <http://rmpiro.net/decompTumor2Sig/>,
<https://github.com/rmpiro/decompTumor2Sig>

BugReports <https://github.com/rmpiro/decompTumor2Sig/issues>

biocViews Software, SNP, Sequencing, DNaseq, GenomicVariation, SomaticMutation, BiomedicalInformatics, Genetics, BiologicalQuestion, StatisticalMethod

VignetteBuilder knitr

RoxygenNote 6.1.1

git_url <https://git.bioconductor.org/packages/decompTumor2Sig>

git_branch RELEASE_3_10

git_last_commit b695d01

git_last_commit_date 2019-10-29

Date/Publication 2020-04-14

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decompTumor2Sig-package

decompTumor2Sig - Decomposition of individual tumors into mutational signatures by signature refitting

Description

The decompTumor2Sig package uses quadratic programming to decompose the somatic mutation catalog from an individual tumor sample (or multiple individual tumor samples) into a set of given mutational signatures (either of the "Alexandrov model" by Alexandrov et al, Nature 500(7463):415-421, 2013, or the "Shiraishi model" by Shiraishi et al, PLoS Genet 11(12):e1005657, 2015), thus computing weights (or "exposures") that reflect the contributions of the signatures to the mutation load of the tumor.

Details

Package: decompTumor2Sig
 Type: Package
 Version: 2.1.0
 Date: 2019-08-18
 License: GPL (>=2)

The package provides the following functions:

<code>composeGenomesFromExposures()</code> :	(re-)construct tumor genome mutation frequencies from the signatures and their corresponding exposures, or contributions.
<code>computeExplainedVariance()</code> :	determine the variance explained by estimated signature contributions (i.e., exposures to signatures).
<code>convertAlexandrov2Shiraishi()</code> :	convert a set of Alexandrov signatures to Shiraishi signatures.
<code>convertGenomesFromVRanges()</code> :	convert a genome or set of genomes from a <code>VariantAnnotation::VRanges</code> object.
<code>decomposeTumorGenomes()</code> :	determine the weights/contributions of a set of signatures to each of a set of individual tumor genomes.
<code>determineSignatureDistances()</code> :	for a given signature compute its distances to each of a set of target signatures.
<code>downgradeShiraishiSignatures()</code> :	downgrade Shiraishi signatures by removing flanking bases and/or the transcription direction.
<code>evaluateDecompositionQuality()</code> :	evaluate the quality of a decomposition by comparing the re-composed (=re-constructed) tumor mutation frequencies to those actually observed in the tumor genome.
<code>getGenomesFromMutFeatData()</code> :	extract the genomes from a <code>MutationFeatureData</code> object as provided by, for example, <code>pmsignature::readMPFile</code> .
<code>getSignaturesFromEstParam()</code> :	extract a set of signatures from an <code>EstimatedParameters</code> object as returned by function <code>getPMSignature</code> of the <code>pmsignature</code> package.
<code>isAlexandrovSet()</code> :	checks whether the input list is compatible with the Alexandrov format (probability vectors).
<code>isExposureSet()</code> :	checks whether the input list is compatible with exposure output obtained from <code>decomposeTumorGenomes</code> .
<code>isShiraishiSet()</code> :	checks whether the input list is compatible with the Shiraishi format (matrices or <code>data.frames</code> of probabilities).
<code>isSignatureSet()</code> :	checks whether the input list is compatible with either the Alexandrov or Shiraishi format.
<code>mapSignatureSets()</code> :	find a mapping from one signature set to another.
<code>plotDecomposedContribution()</code> :	plot the decomposition of a genome into mutational signatures

plotExplainedVariance():	(i.e., the contributions of, or exposures to, the signatures). plot the variance of a genome's mutation patterns which can be explained with an increasing number of signatures.
plotMutationDistribution():	plot a single signature or the mutation frequency data for a single genome.
readAlexandrovSignatures():	read Alexandrov signatures in the COSMIC format from a flat file or URL.
readGenomesFromMPF():	read a genome or set of genomes from a Mutation Position Format (MPF) file.
readGenomesFromVCF():	read a genome or set of genomes from a Variant Call Format (VCF) file.
readShiraishiSignatures():	read Shiraishi signatures from flat files.
sameSignatureFormat():	checks whether two input lists are sets of signatures of the same format.

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

composeGenomesFromExposures

Compose tumor genomes from exposures.

Description

'composeGenomesFromExposures()' re-composes (or predicts) tumor genomes (i.e., their mutation frequencies) from the given mutational signatures and their corresponding exposures, or contributions. The (re-)composition is performed by computing the weighted sum of the mutational signatures, where the weights are the exposures (=contributions) of the corresponding signatures. This can, for example, be used to verify that a decomposition obtained from decomposeTumorGenomes is meaningful.

Usage

```
composeGenomesFromExposures(exposures, signatures)
```

Arguments

exposures (Mandatory) A single vector or list of vectors containing the estimated signature contributions/exposures as computed by the function `decomposeTumorGenomes`. A list of vectors is used if the (re-)composition shall be performed for multiple genomes. The number of elements of each exposure vector must correspond to the number of signatures.

signatures (Mandatory) The list of signatures (vectors, data frames or matrices) for which the exposures were obtained. Each of the list objects represents one mutational signature. Vectors are used for Alexandrov signatures, data frames or matrices for Shiraishi signatures.

Value

A list of "predicted" genomes, i.e., the frequencies of their mutational patterns computed as weighted sums of the mutational signatures, where the weights correspond to the contributions of, i.e., exposures to, the corresponding signatures.

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References

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See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load preprocessed breast cancer genomes (object 'genomes') from
### Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
                    "Nik-Zainal_PMIID_22608084-genomes-Alexandrov_3bases.Rdata",
```

```
    package="decompTumor2Sig")
load(gfile)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

### re-compose (predict) tumor genome features from exposures
predGenomes <- composeGenomesFromExposures(exposures, signatures)
```

computeExplainedVariance

Compute the explained variance.

Description

'computeExplainedVariance()' computes for one or more tumors the variance which is explained by the estimated contributions (exposures) of a set of signatures when compared to the observed genomes.

Usage

```
computeExplainedVariance(exposures, signatures, genomes)
```

Arguments

exposures	(Mandatory) A single vector or list of vectors containing the estimated signature contributions/exposures as provided by the function decomposeTumorGenomes. A list of vectors is used if the explained variance shall be computed for multiple genomes. The number of exposure vectors must correspond to the number of genomes. The number of elements of each exposure vector must correspond to the number of signatures.
signatures	(Mandatory) The list of signatures (vectors, data frames or matrices) for which the exposures were obtained. Each of the list objects represents one mutational signature. Vectors are used for Alexandrov signatures, data frames or matrices for Shiraishi signatures.
genomes	(Mandatory) Can be either a vector, a data frame or a matrix (for an individual tumor genome), or a list of one of these object types (for multiple tumors). Each tumor genome must be of the same form as the signatures.

Value

A numeric vector of explained variances, one for each genome.

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References

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See Also

[decompTumor2Sig](#)

[decomposeTumorGenomes](#)

[plotExplainedVariance](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load preprocessed breast cancer genomes (object 'genomes') from
### Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
                    "Nik-Zainal_PMIID_22608084-genomes-Alexandrov_3bases.Rdata",
                    package="decompTumor2Sig")
load(gfile)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

### compute explained variance for the tumor genomes
computeExplainedVariance(exposures, signatures, genomes)
```

convertAlexandrov2Shiraishi

Convert Alexandrov-type signatures to Shiraishi signatures

Description

'convertAlexandrov2Shiraishi()' converts a set Alexandrov signatures to the Shiraishi model, summing the respective frequencies of base changes, and upstream and downstream flanking bases. In most cases, the resulting Shiraishi signatures don't provide information on the transcription strand, as this is not part of the standard Alexandrov signatures. While the conversion is mainly thought for signatures, it actually works also for mutation frequency data from genomes which have the same format. [Attention: this conversion entails a loss of specificity and the applicability of Shiraishi signatures derived from Alexandrov signatures has not been extensively explored!]

Usage

```
convertAlexandrov2Shiraishi(signatures)
```

Arguments

signatures (Mandatory) A list of Alexandrov signatures with named elements as produced by readAlexandrovSignatures.

Value

A list of Shiraishi signatures that can be used for decomposeTumorGenomes.

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[readAlexandrovSignatures](#)
[readShiraishiSignatures](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

### convert them to the Shiraishi model
signShiraishi <- convertAlexandrov2Shiraishi(signAlexandrov)
```

convertGenomesFromVRanges

Convert genomes from a VRanges object

Description

'convertGenomesFromVRanges()' converts the SNVs of a single tumor genome (sample) or a set of genomes from a VRanges object (package VariantAnnotation) and determines the mutation frequencies according to a specific model of mutational signatures (Alexandrov or Shiraishi), such that the resulting format can be used as genomes input for decomposeTumorGenomes.

Usage

```
convertGenomesFromVRanges(vranges, numBases=5, type="Shiraishi",
trDir=TRUE, enforceUniqueTrDir=TRUE,
refGenome=BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19,
transcriptAnno=
TxDb.Hsapiens.UCSC.hg19.knownGene::TxDb.Hsapiens.UCSC.hg19.knownGene,
verbose=TRUE)
```

Arguments

vranges	(Mandatory) The VRanges object which specifies the mutations.
numBases	(Mandatory) Total number of bases (mutated base and flanking bases) to be used for sequence patterns. Must be odd. Default: 5
type	(Mandatory) Signature model or type ("Alexandrov" or "Shiraishi"). Default: "Shiraishi"
trDir	(Mandatory) Specifies whether the transcription direction is taken into account in the signature model. If so, only mutations within genomic regions with a defined transcription direction can be considered. Default: TRUE
enforceUniqueTrDir	(Optional) Used only if trDir is TRUE. If enforceUniqueTrDir is TRUE (default), then mutations which map to a region with multiple overlapping genes with opposing transcription directions will be excluded from the analysis. If FALSE, the transcript direction encountered first in the transcript database (see transcriptAnno) is assigned to the mutation. The latter was the behavior until version 1.3.5 of decompTumor2Sig and is also the behavior of pmsignature. However, it is preferable to exclude these mutations from the count (default) because from mutation data alone it cannot be inferred which of the two genes has the higher transcriptional activity which might potentially be linked to the occurrence of the mutation. (If you are unsure, use the default setting; this option exists mostly for backward compatibility with older versions.)
refGenome	(Mandatory) The reference genome (BSgenome) needed to extract sequence patterns. Default: BSgenome object for hg19.
transcriptAnno	(Optional) Transcript annotation (TxDb object) used to determine the transcription direction. This is required only if trDir is TRUE. Default: TxDb object for hg19.
verbose	(Optional) Print information about reading and processing the mutation data. Default: TRUE

Value

A list containing the genomes in terms of frequencies of the mutated sequence patterns. This list of genomes can be used for decomposeTumorGenomes.

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See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)
[readGenomesFromVCF](#)
[readGenomesFromMPF](#)
[getGenomesFromMutFeatData](#)

Examples

```
### load the reference genome and the transcript annotation database
refGenome <- BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19
transcriptAnno <-
  TxDb.Hsapiens.UCSC.hg19.knownGene::TxDb.Hsapiens.UCSC.hg19.knownGene

### take the breast cancer genomes from Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-VCF-convertedfromMPF.vcf.gz",
  package="decompTumor2Sig")

### get the corresponding VRanges object (using the VariantAnnotation
### package)
library(VariantAnnotation)
vr <- readVcfAsVRanges(gfile, genome="hg19")

### convert the VRanges object to the decompTumor2Sig format
genomes <- convertGenomesFromVRanges(vr, numBases=5, type="Shiraishi",
  trDir=TRUE, enforceUniqueTrDir=TRUE, refGenome=refGenome,
  transcriptAnno=transcriptAnno, verbose=FALSE)
```

decomposeTumorGenomes *Decompose tumor genomes into mutational signatures*

Description

`'decomposeTumorGenomes()'` is the core function of this package. It decomposes tumor genomes into a given set of mutational signatures by computing their contributions (exposures) to the mutational load via quadratic programming. The function takes a set of mutational signatures and the mutation features of one or more tumor genomes and computes weights, i.e., contributions for each of the signatures in each individual genome. Alternatively, the function can determine for each genome only a subset of signatures whose contributions are sufficient to exceed a user-given minimum threshold for the explained variance of the genome's mutation patterns.

Usage

```
decomposeTumorGenomes(genomes, signatures, minExplainedVariance=NULL,
minNumSignatures=2, maxNumSignatures=NULL, greedySearch=FALSE,
constrainToMaxContribution=FALSE, tolerance=0.1, verbose=FALSE)
```

Arguments

- genomes** (Mandatory) Can be either a vector, a data frame or a matrix (for an individual tumor genome), or a list of one of these object types (for multiple tumors). Each tumor genome must be of the same form as the signatures.
- signatures** (Mandatory) A list of vectors, data frames or matrices. Each of the objects represents one mutational signature. Vectors are used for Alexandrov signatures, data frames or matrices for Shiraishi signatures.
- minExplainedVariance** (Optional) If NULL (default), exactly `maxNumSignatures` (see below; default: all) will be taken for decomposing each genome. If a numeric value between 0 and 1 is specified for `minExplainedVariance`, for each genome the function will select the smallest number of signatures which is sufficient to explain at least the specified fraction of the variance of the genome's mutation patterns. E.g., if `minExplainedVariance=0.99` the smallest subset of signatures that explains at least 99% of the variance is taken. Please note: depending on the number of signatures, this may take quite a while because by default for each number `K` of signatures, all possible subsets composed of `K` signatures will be tested to identify the subset that explains the highest part of the variance. If not enough variance is explained, `K` will be incremented by one. Notes: 1) to speed up the search, the parameters `minNumSignatures`, `maxNumSignatures` and `greedySearch` can be used; 2) for genomes for which none of the possible subsets of signatures explains enough variance, the returned exposure vector will be set to NULL.
- minNumSignatures** (Optional) Used if `minExplainedVariance` is specified (see above). To find the smallest subset of signatures which explain the variance, at least this number of signatures will be taken. This can be used to reduce the search space in a time-consuming search over a large number of signatures.
- maxNumSignatures** (Optional) If `minExplainedVariance` is specified to find the smallest subset of signatures which explain the variance, at most `maxNumSignatures` will be taken. This can be used to reduce the search space in a time-consuming search over a large number of signatures. If `minExplainedVariance` is NULL, then exactly `maxNumSignatures` signatures will be used. The default for `maxNumSignatures` is NULL (all signatures).
- greedySearch** (Optional) Used only in case `minExplainedVariance` has been specified. If `greedySearch` is TRUE then not all possible combinations of `minNumSignatures` to `maxNumSignatures` signatures will be checked. Instead, first all possible combinations for exactly `minNumSignatures` will be checked to select the best starting set, then iteratively the next best signature will be added (maximum increase in explained variability) until `minExplainedVariance` of the variance can be explained (or `maxNumSignatures` is exceeded). NOTE: this approximate search is highly recommended for large sets of signatures (>15)!
- constrainToMaxContribution** (Optional) [Note: this is EXPERIMENTAL and is usually not needed!] If TRUE, the maximum contribution that can be attributed to a signature will be constraint

by the variant feature counts (e.g., specific flanking bases) observed in the individual tumor genome. If, for example, 30% of all observed variants have a specific feature and 60% of the variants produced by a mutational process/signature will manifest the feature, then the signature can have contributed up to $0.3/0.6$ ($=0.5$ or 50%) of the observed variants. The lowest possible contribution over all signature features will be taken as the allowed maximum contribution of the signature. This allowed maximum will additionally be increased by the value specified as `tolerance` (see below). For the illustrated example and `tolerance=0.1` a contribution of up to $0.5+0.1 = 0.6$ (or 60%) of the signature would be allowed.

<code>tolerance</code>	(Optional) If <code>constrainToMaxContribution</code> is TRUE, the maximum contribution computed for a signature is increased by this value (see above). If the parameter <code>constrainToMaxContribution</code> is FALSE, the tolerance value is ignored. Default: 0.1.
<code>verbose</code>	(Optional) If TRUE some information about the processed genome and used number of signatures will be printed.

Value

A list of signature weight vectors (also called 'exposures'), one for each tumor genome. E.g., the first vector element of the first list object is the weight/contribution of the first signature to the first tumor genome. **IMPORTANT:** If `minExplainedVariance` is specified, then the exposures of a genome will NOT be returned if the minimum explained variance is not reached within the requested minimum and maximum numbers of signatures (`minNumSignatures` and `maxNumSignatures`)! The corresponding exposure vector will be set to NULL.

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References

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 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load reference genome
refGenome <- BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19
```

```

### read breast cancer genomes from Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-VCF-convertedfromMPF.vcf.gz",
  package="decompTumor2Sig")
genomes <- readGenomesFromVCF(gfile, numBases=3, type="Alexandrov",
  trDir=FALSE, refGenome=refGenome, verbose=FALSE)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

### (for further examples on searching subsets, please see the vignette)

```

determineSignatureDistances

Determine differences between a given signature and a set of target signatures.

Description

`determineSignatureDistances()` determines all distances (i.e., differences) between a given signature (of type Alexandrov or Shiraishi) and a set of target signatures (of the same type). This can help to compare signatures that have been determined in different ways or from different datasets. Different distance measures can be used (see details below).

Usage

```

determineSignatureDistances(fromSignature, toSignatures,
  method="euclidean")

```

Arguments

`fromSignature` (Mandatory) A single signature of the Alexandrov (vector) or Shiraishi type (data frame or matrix).

`toSignatures` (Mandatory) The list of target signatures for which to compute the distances to `fromSignature`. These target signatures must be of the same type and format as `fromSignature`.

`method` (Optional) The distance measure to be used. This can be one of the following: "frobenius" for Frobenius distance between matrices (only for Shiraishi signatures); "rss" for the residual sum of squares (squared error); or any distance measure available for the function `dist` of the `stats` package. Default: "euclidean".

Details

Distances that can be used are:

"frobenius"	Forbenius distance between real-valued matrices (or Shiraishi signatures) A and B: $F = \sqrt{\text{trace}((A-B) \%*\% t(A-B))}$
"rss"	Residual sum of squares (i.e., squared error): $\text{rss} = \text{sum}((A-B)^2)$

"euclidean" (see ?dist for details)
 "maximum" (see ?dist for details)
 "manhattan" (see ?dist for details)
 "canberra" (see ?dist for details)
 "binary" (see ?dist for details)
 "minkowski" (see ?dist for details)

Value

A signature-named vector containing all distances. This vector has the same order as the target signature list, so it is not sorted according to distance.

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References

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 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[mapSignatureSets](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

### convert them to Shiraishi signatures
signAlex2Shi <- convertAlexandrov2Shiraishi(signAlexandrov)

### define an arbitrary signature just for testing
### (similar to signature 1)
testSig <- matrix(c(0.1, 0, 0.7, 0.1, 0.1, 0,
                  0.3, 0.2, 0.3, 0.2, 0, 0,
                  0.2, 0.1, 0.5, 0.2, 0, 0), nrow=3, byrow=TRUE)

### compute distances of the test signature to the converted
### Alexandrov signatures from COSMIC
determineSignatureDistances(testSig, signAlex2Shi, method="frobenius")
```

`downgradeShiraishiSignatures`*Downgrade Shiraishi-type signatures.*

Description

‘downgradeShiraishiSignatures()’ downgrades/trims signatures of the Shiraishi type by discarding flanking bases (reducing the length of the sequence pattern) and/or the transcription direction. The downgrade doesn’t pose a problem because the flanking bases and the transcription direction are considered as independent features according to the Shiraishi model of mutational signatures.

Usage

```
downgradeShiraishiSignatures(signatures, numBases=NULL,  
removeTrDir=FALSE)
```

Arguments

<code>signatures</code>	(Mandatory) A list of Shiraishi signatures that need to be downgraded/trimmed.
<code>numBases</code>	(Conditionally optional) The total number of bases (mutated base plus flanking bases around the mutated base) that should be kept. All further flanking bases farther away from the mutated bases are dropped. If specified, <code>numBases</code> must be odd and smaller than the current number of bases of the signatures. If NULL, no flanking bases will be dropped. At least one of <code>numBases</code> or <code>removeTrDir</code> must be specified.
<code>removeTrDir</code>	(Conditionally optional) Logical value that specifies whether information on the transcript direction should be dropped (if present at all). At least one of <code>numBases</code> or <code>removeTrDir</code> must be specified.

Value

A list of Shiraishi signatures that have been accordingly downgraded.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)

Examples

```
### Load 15 Shiraishi signatures obtained from 435 tumor genomes from
### Alexandrov et al. (number of bases: 5, transcription direction: yes)
sfile <- system.file("extdata",
  "Alexandrov_PMIID_23945592_435_tumors-pmsignature-15sig.Rdata",
  package="decompTumor2Sig")
load(sfile)

### downgrade the signatures to include only 3 bases and drop the
### transcription direction
downgradeShiraishiSignatures(signatures, numBases=3, removeTrDir=TRUE)
```

```
evaluateDecompositionQuality
```

Evaluate tumor decomposition quality.

Description

‘evaluateDecompositionQuality()’ evaluates the quality of the decomposition into exposures of a single tumor. The function evaluates the quality of a decomposition obtained from the function `decomposeTumorGenomes` by comparing the re-composed (=re-constructed) tumor genome mutation frequencies to those actually observed in the tumor genome. Tumor genome mutation frequencies are reconstructed using `composeGenomesFromExposures` and the results can optionally be plotted.

Usage

```
evaluateDecompositionQuality(exposure, signatures, genome,
  plot=FALSE)
```

Arguments

exposure	(Mandatory) A single vector containing the estimated signature contributions, or exposures, of a single tumor as provided by <code>decomposeTumorGenomes</code> . The number of elements of the exposure vector must correspond to the number of signatures (see below).
signatures	(Mandatory) The list of signatures (vectors, data frames or matrices) for which the exposures were obtained. Each of the list objects represents one mutational signature. Vectors are used for Alexandrov signatures, data frames or matrices for Shiraishi signatures.
genome	(Mandatory) A single tumor genome in form of mutation frequencies specified either in the Alexandrov or the Shiraishi format (must match the format used for signatures, see above).
plot	(Optional) If FALSE (default), the numerical results (see below) will be returned. If TRUE, the reconstructed mutation frequencies will be plotted against the original, observed mutation frequencies and the numerical results will be integrated as text labels in the plot.

Value

A named list object containing measurements for the Pearson correlation coefficient between the reconstructed and observed mutation frequencies, and the explained variance; or alternatively, a plot with these measurements (see option `plot` above).

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) `decompTumor2Sig`: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)
[composeGenomesFromExposures](#)
[computeExplainedVariance](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load preprocessed breast cancer genomes (object 'genomes') from
### Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-genomes-Alexandrov_3bases.Rdata",
  package="decompTumor2Sig")
load(gfile)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

### evaluate the decomposition by comparing to the original data
evaluateDecompositionQuality(exposures[[1]], signatures, genomes[[1]])
```

`getGenomesFromMutFeatData`*Get genomes (mutation frequencies) from MutationFeatureData.*

Description

`'getGenomesFromMutFeatData()'` takes a `MutationFeatureData` object (mutation count data) as read by the `'pmsignature'` package (e.g., by `pmsignature::readMPFile`, version 0.3.0) and extracts the mutation counts of the genomes therein. For passing the genomes to `decomposeTumorGenomes`, the mutation counts must be normalized to mutation frequencies, which is done by default. [IMPORTANT: set `normalize` to `FALSE` only if you are interested in full integer counts, but do not pass unnormalized counts to `decomposeTumorGenomes!`]

Usage

```
getGenomesFromMutFeatData(mutFeatData, normalize=TRUE)
```

Arguments

<code>mutFeatData</code>	(Mandatory) A <code>MutationFeatureData</code> object as constructed, for example, by <code>pmsignature::readMPFile</code> .
<code>normalize</code>	(Optional) Boolean value to specify whether to normalize the mutation count data to mutation fractions between 0 and 1. This is the default and NECESSARY in case you want to pass the return value to <code>decomposeTumorGenomes</code> . Set <code>normalize</code> to <code>FALSE</code> only if you are interested in full integer counts, but do not pass unnormalized counts to <code>decomposeTumorGenomes!</code>

Value

A list of mutation frequencies (or mutation counts if not normalized), one object per genome. The format is either according to the Shiraishi or the Alexandrov model, depending on how the mutation data was loaded with `pmsignature`.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) `decompTumor2Sig`: Identification of mutational signatures active in individual tumors. *BMC Bioinformatics* (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. *NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era*, October 16-18, 2017, Palermo, Italy. *PeerJ Preprints* 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)

Examples

```
### get breast cancer genomes from
### Nik-Zainal et al (PMID: 22608084) in the format produced by
### pmsignature (PMID: 26630308)
pmsigdata <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-pmsignature-G.Rdata",
  package="decompTumor2Sig")
load(pmsigdata)

### extract the genomes from the pmsignature G object
genomes <- getGenomesFromMutFeatData(G, normalize=TRUE)
```

```
getSignaturesFromEstParam
```

Get signatures from an EstimatedParameters object.

Description

'getSignaturesFromEstParam()' takes an EstimatedParameters object (signatures data) as computed by the 'pmsignature' package (by pmsignature::getPMSignature; version 0.3.0) and extracts the signature information. The signatures can then be passed to decomposeTumorGenomes.

Usage

```
getSignaturesFromEstParam(Param)
```

Arguments

Param (Mandatory) A pmsignature::EstimatedParameters object as those produced by the de novo signature construction method pmsignature::getPMSignature.

Value

A list of Shiraishi signatures, one object per signature. Please see readShiraishiSignatures or the decompTumor2Sig vignette for more information on the format of Shiraishi signatures.

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[readShiraishiSignatures](#)

Examples

```
### load signatures for breast cancer genomes from
### Nik-Zainal et al (PMID: 22608084) in the format produced by
### pmsignature (PMID: 26630308)
pmsigdata <- system.file("extdata",
                        "Nik-Zainal_PMIID_22608084-pmsignature-Param.Rdata",
                        package="decompTumor2Sig")
load(pmsigdata)

### extract the signatures from the pmsignature Param object
signatures <- getSignaturesFromEstParam(Param)
```

isAlexandrovSet

isAlexandrovSet

Description

'isAlexandrovSet()' checks whether the input object is a set (list) of numeric objects compatible with the Alexandrov format (probability vectors; sum up to 1). NOTE: These can also be genomes compatible with the Alexandrov format!

Usage

```
isAlexandrovSet(x)
```

Arguments

x Object to be checked.

Value

Logical value (true or false).

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>

Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).

Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[readAlexandrovSignatures](#)
[isSignatureSet](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

isAlexandrovSet(signAlexandrov)
```

isExposureSet

isExposureSet

Description

'isExposureSet()' checks whether the input object is a set (list) of numeric objects compatible with exposure output obtained from decomposeTumorGenomes.

Usage

```
isExposureSet(x)
```

Arguments

x Object to be checked.

Value

Logical value (true or false).

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>

Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).

Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load reference genome
refGenome <- BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19

### read breast cancer genomes from Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-VCF-convertedfromMPF.vcf.gz",
  package="decompTumor2Sig")
genomes <- readGenomesFromVCF(gfile, numBases=3, type="Alexandrov",
  trDir=FALSE, refGenome=refGenome, verbose=FALSE)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

isExposureSet(exposures)
```

isShiraishiSet

isShiraishiSet

Description

'isShiraishiSet()' checks whether the input object is a set (list) of numeric objects compatible with the Shiraishi format (matrices or data.frames of probabilities; 6 columns, each row sums up to 1). NOTE: These can also be genomes compatible with the Shiraishi format!

Usage

```
isShiraishiSet(x)
```

Arguments

x Object to be checked.

Value

Logical value (true or false).

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[isSignatureSet](#)
[readShiraishiSignatures](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

### convert them to the Shiraishi model
signShiraishi <- convertAlexandrov2Shiraishi(signAlexandrov)

isShiraishiSet(signShiraishi)
```

isSignatureSet	<i>isSignatureSet</i>
----------------	-----------------------

Description

'isSignatureSet()' checks whether the input object is a set (list) of numeric objects compatible with either the Alexandrov format (probability vectors; see isAlexandrovSet) or the Shiraishi format (matrices or data.frames of probabilities; see isShiraishiSet). NOTE: These can also be genomes compatible with one of the two formats!

Usage

```
isSignatureSet(x)
```

Arguments

x Object to be checked.

Value

Logical value (true or false).

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[isAlexandrovSet](#)
[isShiraishiSet](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

isSignatureSet(signAlexandrov)
```

<code>mapSignatureSets</code>	<i>Map one signature set to another.</i>
-------------------------------	--

Description

‘mapSignatureSets()’ determines a mapping from one set of signatures to another. Both Alexandrov and Shiraishi signatures can be handled, but both sets must be of the same type. The mapping can either be a unique (one-to-one) mapping or identify best matches while allowing multiple signatures to be mapped to the same target signature if it is the best match for more than one signature. Different distance measures can be used (see details below).

Usage

```
mapSignatureSets(fromSignatures, toSignatures, method="euclidean",
  unique=FALSE)
```

Arguments

`fromSignatures` (Mandatory) A set (list) of signatures of the Alexandrov (vector) or Shiraishi type (data frame or matrix), that has to be mapped to the signatures of a second set (`toSignatures`).

`toSignatures` (Mandatory) The set (list) of signatures to which the set of `fromSignatures` has to be mapped.

method	(Optional) The distance measure to be used. This can be one of the following: "frobenius" for Frobenius distance between matrices (only for Shiraishi signatures); "rss" for the residual sum of squares (squared error); or any distance measure available for the function <code>dist()</code> of the <code>stats</code> package. Default: "euclidean".
unique	(Optional) If set to <code>FALSE</code> (default), then for each signature of <code>fromSignatures</code> the best match (minimum distance) from <code>toSignatures</code> is selected. The selected signatures need not be unique, i.e., one signature of <code>toSignatures</code> may be the best match for multiple signatures of <code>fromSignatures</code> . If set to <code>TRUE</code> , i.e., if a unique (one-to-one) mapping is required, an iterative approach is performed: in each step, the best matching pair from <code>fromSignatures</code> and <code>toSignatures</code> is mapped and then removed from the list of signatures that remain to be mapped, such that they cannot be selected again.

Details

Distances that can be used are:

"frobenius"	Forbenius distance between real-valued matrices (or Shiraishi signatures) A and B: $F = \sqrt{\text{trace}((A-B) \%*\% t(A-B))}$
"rss"	Residual sum of squares (i.e., squared error): $\text{rss} = \text{sum}((A-B)^2)$
"euclidean"	(see <code>?dist</code> for details)
"maximum"	(see <code>?dist</code> for details)
"manhattan"	(see <code>?dist</code> for details)
"canberra"	(see <code>?dist</code> for details)
"binary"	(see <code>?dist</code> for details)
"minkowski"	(see <code>?dist</code> for details)

Value

A vector having as elements the mapped signatures of `toSignatures`, and as names the signatures of `fromSignatures` with which they have been associated.

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) `decompTumor2Sig`: Identification of mutational signatures active in individual tumors. *BMC Bioinformatics* (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. *NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era*, October 16-18, 2017, Palermo, Italy. *PeerJ Preprints* 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[determineSignatureDistances](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

### convert them to Shiraishi signatures
signAlex2Shi <- convertAlexandrov2Shiraishi(signAlexandrov)

### define a small set of arbitrary signatures just for testing
### (similar to signatures 1, 5 and 13, respectively)
test1 <- matrix(c( 0.1, 0, 0.7, 0.1, 0.1, 0,
                  0.3, 0.2, 0.3, 0.2, 0, 0,
                  0.2, 0.1, 0.5, 0.2, 0, 0 ), nrow=3, byrow=TRUE)

test2 <- matrix(c( 0.1, 0.1, 0.3, 0.1, 0.3, 0.1,
                  0.3, 0.25, 0.2, 0.25, 0, 0,
                  0.3, 0.2, 0.2, 0.3, 0, 0 ), nrow=3, byrow=TRUE)

test3 <- matrix(c( 0.1, 0.7, 0.2, 0, 0, 0,
                  0, 0, 0, 1.0, 0, 0,
                  0.5, 0.1, 0, 0.4, 0, 0 ), nrow=3, byrow=TRUE)

fromSig <- list(sig1=test1, sig2=test2, sig3=test3)

### compute distances of the test signature to the converted
### Alexandrov signatures from COSMIC
mapSignatureSets(fromSig, signAlex2Shi, method="frobenius", unique=TRUE)
```

plotDecomposedContribution

Plot the decomposition (contributions/exposures) of a tumor genome.

Description

'plotDecomposedContribution()' plots the decomposition of a tumor genome, i.e., the contributions/exposures obtained from decomposeTumorGenomes for a set of signatures.

Usage

```
plotDecomposedContribution(decomposition, signatures=NULL,
removeNA=TRUE)
```

Arguments

decomposition (Mandatory) A decomposition vector (exposure vector) obtained for a single tumor genome.

signatures	(Optional) A list object containing the signatures used to compute the decomposition. If specified, the signature labels used in the plot will be taken from the element names of the list; otherwise signature names will be taken from the exposure object (decomposition) or named from sign_1 to sign_N.
removeNA	(Optional) If TRUE (default), signatures with an NA as exposure will not be included on the x-axis of the the plot. Exposures can be NA if they have been determined with a greedy search.

Value

Returns (or draws) a plot of the decomposed tumor genome (i.e., contributions of the single signatures).

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### load preprocessed breast cancer genomes (object 'genomes') from
### Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
                    "Nik-Zainal_PMIID_22608084-genomes-Alexandrov_3bases.Rdata",
                    package="decompTumor2Sig")
load(gfile)

### compute exposures
exposures <- decomposeTumorGenomes(genomes, signatures, verbose=FALSE)

### plot signature composition of the first genome
plotDecomposedContribution(exposures[[1]], signatures=NULL)
```

plotExplainedVariance *Plot the explained variance as a function of the number of signatures*

Description

'plotExplainedVariance()' plots the explained variance of a single tumor genome's mutation patterns as a function of the number of signatures (increasing subsets of signatures) used for decomposition. For each number K of signatures, the highest variance explained by possible subsets of K signatures will be plotted (full or greedy search, see below). This can help to evaluate what minimum threshold for the explained variance can be used to decompose tumor genomes with the function decomposeTumorGenomes.

Usage

```
plotExplainedVariance(genome, signatures, minExplainedVariance=NULL,
minNumSignatures=2, maxNumSignatures=NULL, greedySearch=FALSE)
```

Arguments

- | | |
|----------------------|--|
| genome | (Mandatory) The mutation load of a single genome in Alexandrov- or Shiraishi-format, i.e. as vector or matrix. The format must be the same as the one used for the signatures (see below). |
| signatures | (Mandatory) The list of signatures (vectors, data frames or matrices) which are to be evaluated. Each of the list objects represents one mutational signature. Vectors are used for Alexandrov signatures, data frames or matrices for Shiraishi signatures. |
| minExplainedVariance | (Optional) If a numeric value between 0 and 1 is specified, the plot highlights the smallest subset of signatures which is sufficient to explain at least the specified fraction of the variance of the genome's mutation patterns. If, for example, minExplainedVariance is 0.99 the smallest subset of signatures that explains at least 99% of the variance will be highlighted. |
| minNumSignatures | (Optional) The plot will be generated only for $K \geq \text{minNumSignatures}$. |
| maxNumSignatures | (Optional) The plot will be generated only for $K \leq \text{maxNumSignatures}$. |
| greedySearch | (Optional) If greedySearch is set to TRUE then not all possible combinations of minNumSignatures to maxNumSignatures signatures will be checked. Instead, first all possible combinations for exactly minNumSignatures will be checked to select the best starting set, then iteratively the next best signature will be added (maximum increase in explained variability) until maxNumSignatures is reached). NOTE: while this is only an approximation, it is highly recommended for large sets of signatures (>15)! |

Value

Returns (or draws) a plot of the explained variance as a function of the number of signatures.

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)
[computeExplainedVariance](#)

Examples

```
### get 15 pre-processed Shiraishi signatures computed (object 'signatures')
### from 435 tumor genomes Alexandrov et al (PMID: 23945592)
### using the pmsignature package
sfile <- system.file("extdata",
  "Alexandrov_PMIID_23945592_435_tumors-pmsignature-15sig.Rdata",
  package="decompTumor2Sig")
load(sfile)

### load preprocessed breast cancer genomes (object 'genomes') from
### Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-genomes-Shiraishi_5bases_trDir.Rdata",
  package="decompTumor2Sig")
load(gfile)

### plot the explained variance for 2 to 6 signatures of the first genome
plotExplainedVariance(genomes[[1]], signatures,
  minExplainedVariance=0.98, minNumSignatures=2, maxNumSignatures=6)
```

plotMutationDistribution

Plot mutation frequency data of a mutational signature or tumor genome.

Description

'plotMutationDistribution()' plots a single signature or the mutation frequency data for a single genome. This works for signatures or genome data of both the Shiraishi and the Alexandrov type.

Usage

```
plotMutationDistribution(mutData, colors = NULL, strip = NULL)
```

Arguments

mutData	(Mandatory) The signature or genome mutation frequency data to be plotted. This can either be a matrix (Shiraishi model) or a numeric vector (Alexandrov model).
colors	Vector of colors to be used for the base change data. For Alexandrov-type data, this vector must contain six elements (one per base change). For Shiraishi-type data, this vector must contain four elements (one per base). If NULL (default), for Alexandrov-type data, the colors are set to those used by the COSMIC website; for Shiraishi-type data, the consensus base colors for sequence logos will be used.
strip	Background color for strip labels; used only for Alexandrov-type data. If NULL (default), "papayawhip" will be used.

Value

Returns (or draws) a plot according to the Alexandrov or Shiraishi model of mutational signatures.

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)

Examples

```
### Attention: using plotMutationDistribution requires the package
### pmsignature to be installed!

### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()

### plot the first Alexandrov signature
plotMutationDistribution(signatures[[1]])
```

```

### read four Shiraishi signatures for breast cancer genomes from
### Nik-Zainal et al (PMID: 22608084) from flat files
sigfiles <- system.file("extdata",
  paste0("Nik-Zainal_PMIID_22608084-pmsignature-sig",1:4, ".tsv"),
  package="decompTumor2Sig")
signatures <- readShiraishiSignatures(sigfiles)

### plot the first Shiraishi signature
plotMutationDistribution(signatures[[1]])

```

```
readAlexandrovSignatures
```

Read Alexandrov-type signatures (COSMIC format).

Description

‘readAlexandrovSignatures()’ reads a set of Alexandrov-type signatures (COSMIC format) from a flat file or URL. Signatures must be specified in the tab-separated format used by the COSMIC website for signatures version 2 (March 2015) or the comma-separated format used for signatures version 3 (May 2019); see details below or http://cancer.sanger.ac.uk/cosmic/signatures_v2 -> "Download signatures" for version 2, or <https://cancer.sanger.ac.uk/cosmic/signatures/SBS/> and <https://www.synapse.org/#!/Synapse:syn12009743> for version 3.

Usage

```
readAlexandrovSignatures(file)
```

Arguments

file (Mandatory) Can be a file name or an URL for download. Default (COSMIC): "https://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt"

Details

For version 3, only Single Base Substitution (SBS) signatures can be used.

COSMIC format for Alexandrov signatures, version 2:

Subst.	Trinucleotide	Mutation Type	Signature 1	Signature 2	...
C>A	ACA	A[C>A]A	0.0110983262	0.0006827082	...
C>A	ACC	A[C>A]C	0.0091493407	0.0006191072	...
C>A	ACG	A[C>A]G	0.0014900705	0.0000992790	...
C>A	ACT	A[C>A]T	0.0062338852	0.0003238914	...
[...]					
T>G	TTG	T[T>G]G	0.0020310769	0.0002066152	...
T>G	TTT	T[T>G]T	0.0040301281	0.0000235982	...

COSMIC/Synapse format for Alexandrov signatures, version 3:

```
Type,SubType,SBS1,SBS2,SBS3,SBS4,SBS5,SBS6, ...
C>A,ACA,8.86E-04,5.80E-07,2.08E-02,4.22E-02,1.20E-02,4.25E-04, ...
C>A,ACC,2.28E-03,1.48E-04,1.65E-02,3.33E-02,9.44E-03,5.24E-04, ...
C>A,ACG,1.77E-04,5.23E-05,1.75E-03,1.56E-02,1.85E-03,5.20E-05, ...
C>A,ACT,1.28E-03,9.78E-05,1.22E-02,2.95E-02,6.61E-03,1.80E-04, ...
[...]
T>G,TTG,5.83E-04,9.54E-05,8.05E-03,2.32E-03,6.94E-03,3.24E-04, ...
T>G,TTT,2.23E-16,2.23E-16,1.05E-02,5.68E-04,1.35E-02,1.01E-03, ...
```

Value

A list of Alexandrov signatures that can be used for `decomposeTumorGenomes`.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
 Krueger, Piro (2018) `decompTumor2Sig`: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
 Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[readShiraishiSignatures](#)

Examples

```
### get Alexandrov signatures from COSMIC
signatures <- readAlexandrovSignatures()
```

`readGenomesFromMPF` *Read tumor genomes from an MPF file (Mutation Position Format).*

Description

`'readGenomesFromMPF()'` reads somatic mutations of a single tumor genome (sample) or a set of genomes from an MPF file (Mutation Position Format; see details below) and determines the mutation frequencies according to a specific model of mutational signatures (Alexandrov or Shiraishi).

Usage

```
readGenomesFromMPF(file, numBases=5, type="Shiraishi", trDir=TRUE,
  enforceUniqueTrDir=TRUE,
  refGenome=BSgenome.Hsapiens.UCSC.hg19:BSgenome.Hsapiens.UCSC.hg19,
  transcriptAnno=
  TxDb.Hsapiens.UCSC.hg19.knownGene:TxDb.Hsapiens.UCSC.hg19.knownGene,
  verbose=TRUE)
```

Arguments

file	(Mandatory) The name of the MPF file (can be compressed with gzip).
numBases	(Mandatory) Total number of bases (mutated base and flanking bases) to be used for sequence patterns. Must be odd. Default: 5
type	(Mandatory) Signature model or type ("Alexandrov" or "Shiraishi"). Default: "Shiraishi"
trDir	(Mandatory) Specifies whether the transcription direction is taken into account in the signature model. If so, only mutations within genomic regions with a defined transcription direction can be considered. Default: TRUE
enforceUniqueTrDir	(Optional) Used only if trDir is TRUE. If enforceUniqueTrDir is TRUE (default), then mutations which map to a region with multiple overlapping genes with opposing transcription directions will be excluded from the analysis. If FALSE, the transcript direction encountered first in the transcript database (see transcriptAnno) is assigned to the mutation. The latter was the behavior until version 1.3.5 of decompTumor2Sig and is also the behavior of pmsignature. However, it is preferable to exclude these mutations from the count (default) because from mutation data alone it cannot be inferred which of the two genes has the higher transcriptional activity which might potentially be linked to the occurrence of the mutation. (If you are unsure, use the default setting; this option exists mostly for backward compatibility with older versions.)
refGenome	(Mandatory) The reference genome (BSgenome) needed to extract sequence patterns. Default: BSgenome object for hg19.
transcriptAnno	(Optional) Transcript annotation (TxDb object) used to determine the transcription direction. This is required only if trDir is TRUE. Default: TxDb object for hg19.
verbose	(Optional) Print information about reading and processing the mutation data. Default: TRUE

Details

An MPF file has the following format (one line per mutation and patient/sample):

```
[sampleID]<tab>[chrom]<tab>[position]<tab>[ref_bases]<tab>[alt_bases]
```

Value

A list containing the genomes in terms of frequencies of the mutated sequence patterns. This list of genomes can be used for decomposeTumorGenomes.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)
[readGenomesFromVCF](#)
[getGenomesFromMutFeatData](#)

Examples

```
### load reference genome and transcript annotation (if direction is needed)
refGenome <- BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19
transcriptAnno <-
  TxDb.Hsapiens.UCSC.hg19.knownGene::TxDb.Hsapiens.UCSC.hg19.knownGene

### read breast cancer genomes from Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata", "Nik-Zainal_PMIID_22608084-MPF.txt.gz",
  package="decompTumor2Sig")
genomes <- readGenomesFromMPF(gfile, numBases=5, type="Shiraishi",
  trDir=TRUE, enforceUniqueTrDir=TRUE, refGenome=refGenome,
  transcriptAnno=transcriptAnno, verbose=FALSE)
```

readGenomesFromVCF *Read tumor genomes from a VCF file (Variant Call Format).*

Description

'readGenomesFromVCF()' reads somatic mutations of a single tumor genome (sample) or a set of genomes from a VCF file (Variant Call Format) and determines the mutation frequencies according to a specific model of mutational signatures (Alexandrov or Shiraishi).

Usage

```
readGenomesFromVCF(file, numBases=5, type="Shiraishi", trDir=TRUE,
  enforceUniqueTrDir=TRUE,
  refGenome=BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19,
  transcriptAnno=
  TxDb.Hsapiens.UCSC.hg19.knownGene::TxDb.Hsapiens.UCSC.hg19.knownGene,
  verbose=TRUE)
```

Arguments

<code>file</code>	(Mandatory) The name of the VCF file (can be compressed with gzip).
<code>numBases</code>	(Mandatory) Total number of bases (mutated base and flanking bases) to be used for sequence patterns. Must be odd. Default: 5
<code>type</code>	(Mandatory) Signature model or type ("Alexandrov" or "Shiraishi"). Default: "Shiraishi"
<code>trDir</code>	(Mandatory) Specifies whether the transcription direction is taken into account in the signature model. If so, only mutations within genomic regions with a defined transcription direction can be considered. Default: TRUE
<code>enforceUniqueTrDir</code>	(Optional) Used only if <code>trDir</code> is TRUE. If <code>enforceUniqueTrDir</code> is TRUE (default), then mutations which map to a region with multiple overlapping genes with opposing transcription directions will be excluded from the analysis. If FALSE, the transcript direction encountered first in the transcript database (see <code>transcriptAnno</code>) is assigned to the mutation. The latter was the behavior until version 1.3.5 of <code>decompTumor2Sig</code> and is also the behavior of <code>pmsignature</code> . However, it is preferable to exclude these mutations from the count (default) because from mutation data alone it cannot be inferred which of the two genes has the higher transcriptional activity which might potentially be linked to the occurrence of the mutation. (If you are unsure, use the default setting; this option exists mostly for backward compatibility with older versions.)
<code>refGenome</code>	(Mandatory) The reference genome (BSgenome) needed to extract sequence patterns. Default: BSgenome object for hg19.
<code>transcriptAnno</code>	(Optional) Transcript annotation (TxDb object) used to determine the transcription direction. This is required only if <code>trDir</code> is TRUE. Default: TxDb object for hg19.
<code>verbose</code>	(Optional) Print information about reading and processing the mutation data. Default: TRUE

Value

A list containing the genomes in terms of frequencies of the mutated sequence patterns. This list of genomes can be used for `decomposeTumorGenomes`.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>

Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).

Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[decomposeTumorGenomes](#)
[readGenomesFromMPF](#)
[getGenomesFromMutFeatData](#)

Examples

```
### load reference genome and transcript annotation (if direction is needed)
refGenome <- BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19
transcriptAnno <-
  TxDb.Hsapiens.UCSC.hg19.knownGene::TxDb.Hsapiens.UCSC.hg19.knownGene

### read breast cancer genomes from Nik-Zainal et al (PMID: 22608084)
gfile <- system.file("extdata",
  "Nik-Zainal_PMIID_22608084-VCF-convertedfromMPF.vcf.gz",
  package="decompTumor2Sig")
genomes <- readGenomesFromVCF(gfile, numBases=5, type="Shiraishi",
  trDir=TRUE, enforceUniqueTrDir=TRUE, refGenome=refGenome,
  transcriptAnno=transcriptAnno, verbose=FALSE)
```

readShiraishiSignatures

Read a set of Shiraishi signatures.

Description

`readShiraishiSignatures()` reads one or more Shiraishi-type signatures from flat files (one file per signature). The signatures must be specified as matrices without headers and row names (see details below).

Usage

```
readShiraishiSignatures(files)
```

Arguments

files (Mandatory) Can be a single file name, a vector of file names, or a list of file names.

Details

Format (see Shiraishi et al. PLoS Genetics 11(12):e1005657, 2015):

First line: Frequencies of the base changes C>A, C>G, C>T, T>A, T>C, and T>G

Following 2k lines (for k up- and downstream flanking bases): Frequencies of the bases A, C, G, and T, followed by two 0 values

Final line (only if transcription direction is considered): Frequencies of occurrences on the transcription strand, and on the opposite strand, followed by four 0 values.

Example:

1.8874e-14	0.10974	0.045918	0.11308	0.07429	0.65697
3.8079e-01	0.12215	0.191456	0.30561	0.00000	0.00000
1.5311e-01	0.34214	0.179774	0.32497	0.00000	0.00000
1.2378e-01	0.10243	0.163461	0.61032	0.00000	0.00000
3.4891e-01	0.15346	0.156687	0.34094	0.00000	0.00000
5.6435e-01	0.43565	0.000000	0.00000	0.00000	0.00000

Value

A list of Shiraishi signatures that can be used for decomposeTumorGenomes.

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>

Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).

Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[readAlexandrovSignatures](#)
[getSignaturesFromEstParam](#)

Examples

```
### read four Shiraishi signatures for breast cancer genomes from
### Nik-Zainal et al (PMID: 22608084) from flat files
sigfiles <- system.file("extdata",
  paste0("Nik-Zainal_PMIID_22608084-pmsignature-sig",1:4, ".tsv"),
  package="decompTumor2Sig")
```

```
signatures <- readShiraishiSignatures(sigfiles)
```

sameSignatureFormat *sameSignatureFormat*

Description

‘sameSignatureFormat()’ checks whether two input object are sets (lists) of numeric objects both compatible with the same signature format (probability vectors for Alexandrov signatures and probability matrices or data.frames for Shiraishi signatures). For Shiraishi signatures also the number of flanking bases and the presence of transcription-strand information are compared. For Alexandrov signatures also the number of triplet changes are compared.

Usage

```
sameSignatureFormat(x, y)
```

Arguments

x	First object to be checked.
y	Second object to be checked.

Value

Logical value (true or false).

Author(s)

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References

<http://rmpiro.net/decompTumor2Sig/>
Krueger, Piro (2018) decompTumor2Sig: Identification of mutational signatures active in individual tumors. BMC Bioinformatics (accepted for publication).
Krueger, Piro (2017) Identification of Mutational Signatures Active in Individual Tumors. NETTAB 2017 - Methods, Tools & Platforms for Personalized Medicine in the Big Data Era, October 16-18, 2017, Palermo, Italy. PeerJ Preprints 5:e3257v1, 2017.

See Also

[decompTumor2Sig](#)
[isAlexandrovSet](#)
[isShiraishiSet](#)

Examples

```
### get Alexandrov signatures from COSMIC
signAlexandrov <- readAlexandrovSignatures()

### convert them to the Shiraishi model
signShiraishi <- convertAlexandrov2Shiraishi(signAlexandrov)

sameSignatureFormat(signAlexandrov, signShiraishi)
```

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