Package 'HiLDA'

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Type Package

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Description A package built under the Bayesian framework of applying hierarchical latent Dirichlet allocation. It statistically tests whether the mutational exposures of mutational signatures (Shiraishi-model signatures) are different between two groups. The package also provides inference and visualization.

License GPL-3

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boundaryTurbo_F *Check whether the parameter F is within the appropriate range*

Description

Check whether the parameter F is within the appropriate range

Usage

```
boundaryTurbo_F(turboF, fdim, signatureNum)
```

Arguments

turboF	F (converted for turboEM)
fdim	a vector specifying the number of possible values for each mutation signature
signatureNum	the number of mutation signatures

Value

a logical value

boundaryTurbo_Q *Check whether the parameter Q is within the appropriate range*

Description

Check whether the parameter Q is within the appropriate range

Usage

```
boundaryTurbo_Q(turboQ, signatureNum, sampleNum)
```

Arguments

turboQ	Q (converted for turboEM)
signatureNum	the number of mutation signatures
sampleNum	the number of cancer genomes

Value

a logical value

`calcPMSLikelihood` *A function for calculating the log-likelihood from the data and parameters*

Description

A function for calculating the log-likelihood from the data and parameters

Usage

```
calcPMSLikelihood(p, y)
```

Arguments

`p`	this variable includes the parameters for mutation signatures and membership parameters
`y`	this variable includes the information on the mutation features, the number of mutation signatures specified and so on

Value

a value

`convertFromTurbo_F` *Restore the converted parameter F for turboEM*

Description

Restore the converted parameter F for turboEM

Usage

```
convertFromTurbo_F(turboF, fdim, signatureNum, isBackground)
```

Arguments

`turboF`	F (converted for turboEM)
`fdim`	a vector specifying the number of possible values for each mutation signature
`signatureNum`	the number of mutation signatures
`isBackground`	the logical value showing whether a background mutaiton features is included or not

Value

a vector

convertFromTurbo_Q *Restore the converted parameter Q for turboEM*

Description

Restore the converted parameter Q for turboEM

Usage

```
convertFromTurbo_Q(turboQ, signatureNum, sampleNum)
```

Arguments

turboQ	Q (converted for turboEM)
signatureNum	the number of mutation signatures
sampleNum	the number of cancer genomes

Value

a vector

convertToTurbo_F *Convert the parameter F so that turboEM can treat*

Description

Convert the parameter F so that turboEM can treat

Usage

```
convertToTurbo_F(vF, fdim, signatureNum, isBackground)
```

Arguments

vF	F (converted to a vector)
fdim	a vector specifying the number of possible values for each mutation signature
signatureNum	the number of mutation signatures
isBackground	the logical value showing whether a background mutaiton features is included or not

Value

a vector

convertToTurbo_Q *Convert the parameter Q so that turboEM can treat*

Description

Convert the parameter Q so that turboEM can treat

Usage

```
convertToTurbo_Q(vQ, signatureNum, sampleNum)
```

Arguments

vQ	Q (converted to a vector)
signatureNum	the number of mutation signatures
sampleNum	the number of cancer genomes

Value

a vector

EstimatedParameters-class *An S4 class representing the estimated parameters*

Description

An S4 class representing the estimated parameters

Slots

sampleList a list of sample names observed in the input mutation data

signatureNum the number of mutation signatures specified at the time of estimation

isBackGround the flag showing whether the background signature data is used or not.

backGroundProb the background signatures

signatureFeatureDistribution estimated parameters for mutation signatures

sampleSignatureDistribution estimated parameters for memberships of mutation signatures for each sample

loglikelihood the log-likelihood value for the estimated parameters

getLogLikelihoodC *Calculate the value of the log-likelihood for given parameters*

Description

Calculate the value of the log-likelihood for given parameters

Usage

```
getLogLikelihoodC(
  vPatternList,
  vSparseCount,
  vF,
  vQ,
  fdim,
  signatureNum,
  sampleNum,
  patternNum,
  samplePatternNum,
  isBackground,
  vF0
)
```

Arguments

vPatternList	The list of possible mutation features (converted to a vector)
vSparseCount	The table showing (mutation feature, sample, the number of mutation) (converted to a vector)
vF	F (converted to a vector)
vQ	Q (converted to a vector)
fdim	a vector specifying the number of possible values for each mutation signature
signatureNum	the number of mutation signatures
sampleNum	the number of cancer genomes
patternNum	the number of possible combinations of all the mutation features
samplePatternNum	the number of possible combination of samples and mutation patternns
isBackground	the logical value showing whether a background mutaiton features is included or not
vF0	a background mutaiton features

Value

a value

`getMutationFeatureVector` *Get mutation feature vector from context sequence data and reference and alternate allele information*

Description

Get mutation feature vector from context sequence data and reference and alternate allele information

Usage

```
getMutationFeatureVector(
  context,
  ref_base,
  alt_base,
  strandInfo = NULL,
  numBases,
  type
)
```

Arguments

`context`	the context sequence data around the mutated position. This shoud be Biostrings::DNAStringSet class
`ref_base`	the reference bases at the mutated position.
`alt_base`	the alternate bases at the mutated position.
`strandInfo`	transcribed strand information at the mutated position. (this is optional)
`numBases`	the number of flanking bases around the mutated position.
`type`	the type of mutation feature vecotr (should be "independent" or "full").

Value

a mutation featuer vector

`hildaBarplot` *Read the raw mutation data with the mutation feature vector format, estimate and plot both mutation signatures and their fractions*

Description

Read the raw mutation data with the mutation feature vector format, estimate and plot both mutation signatures and their fractions

Usage

```
hildaBarplot(
  inputG,
  hildaResult,
  sigOrder = NULL,
  refGroup,
  sortSampleNum = TRUE,
  refName = "Control",
  altName = "Case",
  charSize = 3
)
```

Arguments

inputG	a MutationFeatureData S4 class output by the pmsignature.
hildaResult	a rjags class output by HiLDA.
sigOrder	the order of signatures if needed (default: NULL).
refGroup	the samples in the reference group (default: NULL).
sortSampleNum	whether to sort plots by number of mutations (default: TRUE).
refName	the name of reference group (default: Control)
altName	the name of the other group (default: Case)
charSize	the size of the character on the signature plot (default: 3)

Value

a list of a signature plot and a barplot of mutational exposures

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
inputFile <- system.file("extdata/hildaLocal.rdata", package="HiLDA")
hildaLocal <- readRDS(inputFile)

hildaBarplot(G, hildaLocal, refGroup=1:4)
```

---

hildaDiffPlot *Read the raw mutation data with the mutation feature vector format, estimate and plot both mutation signatures and their fractions*

Description

Read the raw mutation data with the mutation feature vector format, estimate and plot both mutation signatures and their fractions

Usage

```
hildaDiffPlot(inputG, hildaResult, sigOrder = NULL, charSize = 3)
```

Arguments

inputG	a MutationFeatureData S4 class output by the pmsignature.
hildaResult	a rjags class output by HiLDA.
sigOrder	the order of signatures if needed (default: NULL).
charSize	the size of the character on the signature plot (default: 3)

Value

a list of the signature plot and the mean difference plot.

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
inputFile <- system.file("extdata/hildaLocal.rdata", package="HiLDA")
hildaLocal <- readRDS(inputFile)

hildaDiffPlot(G, hildaLocal)
```

---

hildaGlobalResult *Compute the Bayes factor*

Description

Compute the Bayes factor

Usage

```
hildaGlobalResult(jagsOutput, pM1 = 0.5)
```

Arguments

jagsOutput	the output jags file generated by the jags function from the R2jags package.
pM1	the probability of sampling the null (default: 0.5)

Value

a number for the Bayes factor

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
hildaGlobal <- hildaTest(inputG=G, numSig=3, refGroup=1:4, nIter=1000,
localTest=TRUE)
hildaGlobalResult(hildaGlobal)
```

`hildaLocalResult` *Extract the posterior distributions of the mean differences in muational exposures*

Description

Extract the posterior distributions of the mean differences in muational exposures

Usage

```
hildaLocalResult(jagsOutput)
```

Arguments

`jagsOutput`	the output jags file generated by the jags function from the R2jags package.

Value

a data frame that contains the posterior distributions of difference.

Examples

```
inputFile <- system.file("extdata/hildaLocal.rdata", package="HiLDA")
hildaLocal <- readRDS(inputFile)
hildaLocalResult(hildaLocal)
```

`hildaPlotSignature` *Plot mutation signatures from HiLDA output*

Description

Plot mutation signatures from HiLDA output

Usage

```
hildaPlotSignature(hildaResult, sigOrder = NULL, colorList = NULL, ...)
```

Arguments

hildaResult	a rjags class output by HiLDA
sigOrder	the order of signatures if needed (default: NULL)
colorList	a vector of color for mutational exposures barplots
...	additional arguments passed on to visPMS

Value

a plot object containing all mutational signatures

Examples

```
inputFile <- system.file("extdata/hildaLocal.rdata", package="HiLDA")
hildaLocal <- readRDS(inputFile)
hildaPlotSignature(hildaLocal)
```

---

hildaReadMPFile *Read the raw mutation data of Mutation Position Format.*

Description

The mutation position format is tab-delimited text file, where the 1st-5th columns shows sample names, chromosome names, coordinates, reference bases (A, C, G, or T) and the alternate bases (A, C, G, or T), respectively. An example is as follows;

—

sample1 chr1 100 A C

sample1 chr1 200 A T

sample1 chr2 100 G T

sample2 chr1 300 T C

sample3 chr3 400 T C

—

Also, this function usually can accept compressed files (e.g., by gzip, bzip2 and so on) when using recent version of R.

Usage

```
hildaReadMPFile(
  infile,
  numBases = 3,
  trDir = FALSE,
  bs_genome = NULL,
  txdb_transcript = NULL
)
```

Arguments

infile	the path for the input file for the mutation data of Mutation Position Format.
numBases	the number of upstream and downstream flanking bases (including the mutated base) to take into account.
trDir	the index representing whether transcription direction is considered or not. The gene annotation information is given by UCSC knownGene (TxDb.Hsapiens.UCSC.hg19.knownGene object) When trDir is TRUE, the mutations located in intergenic region are excluded from the analysis.
bs_genome	this argument specifies the reference genome (e.g., B Sgenome.Mmusculus.UCSC.mm10 can be used for the mouse genome). See https://bioconductor.org/packages/release/bioc/html/BSgenome.h for the available genome list
txdb_transcript	this argument specified the transcript database (e.g., TxDb.Mmusculus.UCSC.mm10.knownGene can be used for the mouse genome). See https://bioconductor.org/packages/release/bioc/html/AnnotationD for details.

Value

The output is an instance of MutationFeatureData S4 class (which stores summarized information on mutation data). This will be typically used as the initial values for the global test and the local test.

Examples

```
inputFile <- system.file("extdata/esophageal.mp.txt.gz", package="HiLDA")
G <- hildaReadMPFile(inputFile, numBases=5, trDir=TRUE)
```

---

hildaRhat *Output the maximum potential scale reduction statistic of all parameters estimated*

Description

Output the maximum potential scale reduction statistic of all parameters estimated

Usage

```
hildaRhat(jagsOutput)
```

Arguments

jagsOutput	the output jags file generated by the jags function from the R2jags package.

Value

a number for the Rhat statistic.

Examples

```
inputFile <- system.file("extdata/hildaLocal.rdata", package="HiLDA")
hildaLocal <- readRDS(inputFile)
hildaRhat(hildaLocal)
```

`hildaTest` *Apply HiLDA to statistically testing the global difference in burdens of mutation signatures between two groups*

Description

Apply HiLDA to statistically testing the global difference in burdens of mutation signatures between two groups

Usage

```
hildaTest(
  inputG,
  numSig,
  refGroup,
  useInits = NULL,
  sigOrder = NULL,
  nIter = 2000,
  nBurnin = 0,
  pM1 = 0.5,
  localTest = TRUE,
  ...
)
```

Arguments

`inputG`	a MutationFeatureData S4 class output by the pmsignature.
`numSig`	an integer number of the number of mutational signatures.
`refGroup`	the indice indicating the samples in the reference group.
`useInits`	a EstimatedParameters S4 class output by the pmsignature (default: NULL)
`sigOrder`	the order of the mutational signatures.
`nIter`	number of total iterations per chain (default: 2000).
`nBurnin`	length of burn (default: 0).
`pM1`	the probability of sampling the null (default: 0.5)
`localTest`	a logical value (default: TRUE)
`...`	Other arguments passed on to methods.

Value

the output jags file

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))

## with initial values
hildaLocal <- hildaTest(inputG=G, numSig=3, refGroup=1:4, nIter=1000,
localTest=TRUE)
hildaGlobal <- hildaTest(inputG=G, numSig=3, refGroup=1:4, nIter=1000,
localTest=FALSE)
```

MetaInformation-class *An S4 class to represent a mutation meta information common to many data types*

Description

@slot type type of data format (independent, full, custom) @slot flankingBasesNum the number of flanking bases to consider (only applicable for independent and full types) @slot transcriptionDirection the flag representing whether transcription direction is considered or not @slot possibleFeatures a vector representing the numbers of possible values for each mutation feature

---

MutationFeatureData-class *An S4 class representing the mutation data*

Description

An S4 class representing the mutation data

Slots

`featureVectorList` a list of feature vectors actually observed in the input mutation data

`sampleList` a list of sample names observed in the input mutation data

`countData` a matrix representing the number of mutations and samples. The (1st, 2nd, 3rd) columns are for (mutation pattern index, sample index, frequencies).

`mutationPosition` a data frame containing position and mutations

mySquareEM — *A function for estimating parameters using Squared EM algorithm*

Description

A function for estimating parameters using Squared EM algorithm

Usage

```
mySquareEM(p, y, tol = 1e-04, maxIter = 10000)
```

Arguments

p	this variable includes the parameters for mutation signatures and membership parameters
y	this variable includes the information on the mutation features, the number of mutation signatures specified and so on
tol	tolerance for the estimation (when the difference of log-likelihoods become below this value, stop the estimation)
maxIter	the maximum number of iteration of estimation

Value

a list

pmBarplot — *Plot both mutation signatures and their mutational exposures from pmsignature output*

Description

Plot both mutation signatures and their mutational exposures from pmsignature output

Usage

```
pmBarplot(
  inputG,
  inputParam,
  sigOrder = NULL,
  refGroup = NULL,
  sortSampleNum = TRUE,
  refName = "Control",
  altName = "Case",
  charSize = 3
)
```

Arguments

inputG	a MutationFeatureData S4 class output by the pmsignature.
inputParam	a estimatedParameters S4 class output by the pmsignature.
sigOrder	the order of signatures if needed (default: NULL).
refGroup	the samples in the reference group (default: NULL).
sortSampleNum	whether to sort by number of mutations (default: TRUE).
refName	the name of reference group (default: Control).
altName	the name of the other group (default: Case).
charSize	the size of the character on the signature plot (default: 3).

Value

a list of a signature plot and a barplot of mutational exposures

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
Param <- pmgetSignature(G, K = 3)

pmPlots <- pmBarplot(G, Param, refGroup=1:4)
cowplot::plot_grid(pmPlots$sigPlot, pmPlots$propPlot, rel_widths = c(1,3))
```

---

pmgetSignature *Obtain the parameters for mutation signatures and memberships*

Description

Obtain the parameters for mutation signatures and memberships

Usage

```
pmgetSignature(
  mutationFeatureData,
  K,
  numInit = 10,
  tol = 1e-04,
  maxIter = 10000
)
```

Arguments

mutationFeatureData	the mutation data (MutationFeatureData class (S4 class)) by the hildaReadMPFile.
K	the number of mutation signatures
numInit	the number of performing calculations with different initial values
tol	tolerance for the estimation (when the difference of log-likelihoods become below this value, stop the estimation)
maxIter	the maximum number of iteration of estimation

Value

The output is an instance of EstimatedParameters S4 class, which stores estimated parameters and other meta-information, and will be used for saving parameter values and visualizing the mutation signatures and memberships

Examples

```
## After obtaining G (see e.g., hildaReadMPFile function)
load(system.file("extdata/sample.rdata", package="HiLDA"))
Param <- pmgetSignature(G, K = 3)
```

---

pmMultiBarplot *Plot both mutation signatures and their mutational exposures from pmsignature output for more than two groups*

Description

Plot both mutation signatures and their mutational exposures from pmsignature output for more than two groups

Usage

```
pmMultiBarplot(
  inputG,
  inputParam,
  sigOrder = NULL,
  groupIndices,
  sortSampleNum = TRUE,
  charSize = 3
)
```

Arguments

inputG	a MutationFeatureData S4 class output by the pmsignature.
inputParam	a estimatedParameters S4 class output by the pmsignature.
sigOrder	the order of signatures if needed (default: NULL).
groupIndices	a vector of group indicators.
sortSampleNum	an indictor variable on whether samples are sorted by the number of mutations (default: TRUE).
charSize	the size of the character on the signature plot (default: 3)

Value

a list of the signature plot and the mean difference plot.

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
Param <- pmgetSignature(G, K = 3)

pmPlots <- pmMultiBarplot(G, Param, groupIndices=c(1, rep(2,3), rep(3,6)))
cowplot::plot_grid(pmPlots$sigPlot, pmPlots$propPlot, rel_widths = c(1,3))
```

---

pmPlotSignature *Plot mutation signatures from pmsignature output*

Description

Plot mutation signatures from pmsignature output

Usage

```
pmPlotSignature(inputParam, sigOrder = NULL, colorList = NULL, ...)
```

Arguments

inputParam	a estimatedParameters S4 class output by the pmsignature.
sigOrder	the order of signatures if needed (default: NULL).
colorList	a list of color to highlight the signatures (default: NULL).
...	additional arguments passed on to visPMS.

Value

a plot object containing all mutational signatures

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
Param <- pmgetSignature(G, K = 3)
pmPlotSignature(Param)
```

`PMSboundary` *A functional for generating the function checking the parameter (p) is within the restricted conditions or not*

Description

A functional for generating the function checking the parameter (p) is within the restricted conditions or not

Usage

```
PMSboundary(y)
```

Arguments

`y`	this variable includes the information on the mutation features, the number of mutation signatures specified and so on

Value

a functional

`updateMstepFQC` *Update the parameter F and Q (M-step in the EM-algorithm)*

Description

Update the parameter F and Q (M-step in the EM-algorithm)

Usage

```
updateMstepFQC(
  vPatternList,
  vSparseCount,
  nTheta,
  fdim,
  signatureNum,
  sampleNum,
  patternNum,
  samplePatternNum,
  isBackground
)
```

Arguments

vPatternList	The list of possible mutation features (converted to a vector)
vSparseCount	The table showing (mutation feature, sample, the number of mutation) (converted to a vector)
nTheta	The parameters in the distribution
fdim	a vector specifying the number of possible values for each mutation signature
signatureNum	the number of mutation signatures
sampleNum	the number of cancer genomes
patternNum	the number of possible combinations of all the mutation features
samplePatternNum	the number of possible combination of samples and mutation patternns
isBackground	the logical value showing whether a background mutaiton features is included or not

Value

a vector

---

updatePMSParam *A function for updating parameters using EM-algorithm*

Description

A function for updating parameters using EM-algorithm

Usage

```
updatePMSParam(p, y)
```

Arguments

p	this variable includes the parameters for mutation signatures and membership parameters
y	this variable includes the information on the mutation features, the number of mutation signatures specified and so on

Value

a value

`updateTheta_NormalizedC` *Update the auxiliary parameters theta and normalize them so that the summation of each group sums to 1 (E-step), also calculate the current log-likelihood value*

Description

Update the auxiliary parameters theta and normalize them so that the summation of each group sums to 1 (E-step), also calculate the current log-likelihood value

Usage

```
updateTheta_NormalizedC(
  vPatternList,
  vSparseCount,
  vF,
  vQ,
  fdim,
  signatureNum,
  sampleNum,
  patternNum,
  samplePatternNum,
  isBackground,
  vF0
)
```

Arguments

`vPatternList`	The list of possible mutation features (converted to a vector)
`vSparseCount`	The table showing (mutation feature, sample, the number of mutation) (converted to a vector)
`vF`	F (converted to a vector)
`vQ`	Q (converted to a vector)
`fdim`	a vector specifying the number of possible values for each mutation signature
`signatureNum`	the number of mutation signatures
`sampleNum`	the number of cancer genomes
`patternNum`	the number of possible combinations of all the mutation features
`samplePatternNum`	the number of possible combination of samples and mutation patternns
`isBackground`	the logical value showing whether a background mutaiton features is included or not
`vF0`	a background mutaiton features

Value

a value for theta

`visPMS` *visualize probabisitic mutaiton signature for the independent model*

Description

Generate visualization of mutation signatures for the model with substitution patterns and flanking bases represented by the indepenent representation.

Usage

```
visPMS(
  vF,
  numBases,
  baseCol = NA,
  trDir = FALSE,
  charSize = 5,
  isScale = FALSE,
  alpha = 2,
  charLimit = 0.25
)
```

Arguments

`vF`	a matrix for mutation signature
`numBases`	the number of flanking bases
`baseCol`	the colour of the bases (A, C, G, T, plus/minus strand)
`trDir`	the index whether the strand direction is plotted or not
`charSize`	the size of the character
`isScale`	the index whether the height of the flanking base is changed or not
`alpha`	the parameter for the Renyi entropy (applicable only if the isScale is TRUE)
`charLimit`	the limit of char size

Value

a plot of the input mutational signature

Examples

```
load(system.file("extdata/sample.rdata", package="HiLDA"))
Param <- pmgetSignature(G, K = 3)

sig <- slot(Param, "signatureFeatureDistribution")[1,,]
visPMS(sig, numBases = 5, isScale = TRUE)
```

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