Package 'FIREVAT'

October 18, 2019

```
Type Package
Title FIREVAT, FInding REliable Variants without ArTifacts
Description FIREVAT is a variant filtering tool for cancer sequencing data,
      which uses mutational signatures to identify sequencing artifacts and
     low-quality variants.
Version 0.5.7
Authors Andy Jinseok Lee, Hyunbin Kim
Maintainer Andy Jinseok Lee <jinseok.lee@ncc.re.kr>, Hyunbin Kim <khb7840@ncc.re.kr>
Depends R (>= 3.5.0)
Imports data.table,
     rngtools,
     doRNG,
     stringi,
     bedr,
      GA,
     jsonlite,
     yaml,
     lsa,
     ggpubr,
      caTools,
      ggrepel,
      gridExtra,
     ggplot2,
      rmarkdown,
      gtable,
      dplyr,
     extrafont,
      IRanges,
      BSgenome. Hsapiens. UCSC. hg19,
      BSgenome. Hsapiens. UCSC. hg38,
      MutationalPatterns,
      deconstructSigs
biocViews CancerGenomics,
      VariantRefinement,
```

VariantFiltering,
MutationalSignatures,
SomaticMutation,

URL https://github.com/cgab-ncc/FIREVAT

Encoding UTF-8
LazyData true
RoxygenNote 6.1.1
Suggests knitr

VignetteBuilder knitr

License MIT + file LICENSE

${\sf R}$ topics documented:

AnnotateVCFObj
CheckIfVariantRefinementIsNecessary
Chromosome.Names
ComputeZScore
ComputeZScoreEquiValue
DecimalCeiling
Default.Obj.Fn
DefaultFilterToBinary
EnumerateTriNucCounts
Euc.Exp.Weighted.Obj.Fn
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.1
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.2
Euc.Obj.Fn
Exp.Weighted.A.Art.Obj.Fn
Exp.Weighted.A.Ref.Obj.Fn
Exp.Weighted.Obj.Fn.1
$Exp. Weighted. Obj. Fn. 2 \dots $
$Exp. Weighted. Refined. Seq. Art. Only. Obj. Fn \\ \ldots \\ \ldots \\ 13$
FilterByStrandBiasAnalysis
FilterVCF
GenerateConfigObj
GetCOSMICMutSigs
GetCOSMICMutSigsEtiologiesColors
GetCOSMICMutSigsNames
GetGASuggestedSolutions
GetOptimizedSignatures
GetParameterLowerUpperVector
GetPCAWGMutSigs
GetPCAWGMutSigsEtiologiesColors
GetPCAWGMutSigsNames
GetPCAWGPlatinumMutSigs
GetPCAWGPlatinumMutSigsEtiologiesColors

GetPCAWGPlatinumMutSigsNames	. 21
GetSeedForVCF	
InitializeVCF	
Leaky.ReLU.A.Art.Obj.Fn	
Leaky.ReLU.A.Ref.Obj.Fn	
Leaky.ReLU.Obj.Fn	
MakeFilter	
MutaliskParseVCFObj	
MutPatParseRefMutSigs	
MutPatParseVCFObj	
ParameterToBits	
ParseConfigFile	
PCAWG.All.Sequencing.Artifact.Signatures	
PCAWG.Known.Sequencing.Artifact.Signatures	
PCAWG.Platinum.All.Technology.Related.Artifact.Signatures	
PCAWG.Possible.Sequencing.Artifact.Signatures	
PCAWG.Target.Mutational.Signatures	
PerformStrandBiasAnalysis	
PlotMutaliskResults	
PlotMutationTypes	
PlotOptimizationIterations	
PlotSignaturesContProbs	
PlotTable	
PlotTriNucSpectrum	
PlotVCFStatsBoxPlots	
PlotVCFStatsHistograms	
PrepareAnnotationDB	
PrepareArtifactAnnotationTable	
PrepareArtifactStrandBiasTable	
PrepareArtifactualMutsOptimizationIterationsPlot	
PrepareFilterCutoffsTable	
PrepareGeneticAlgorithmParametersTable	
PrepareIdentifiedSignaturesPlot	
PrepareMLEReconstructedSpectrumsPlot	
PrepareNucleotideSubstitutionTypesPlot	. 41
PrepareObservedSpectrumsPlot	
PrepareOptimizationResultsTable	
PrepareOptimizedVCFStatisticsPlot	
PrepareRefinedAnnotationTable	
PrepareRefinedMutsOptimizationIterationsPlot	
PrepareRefinedStrandBiasTable	
PrepareResidualSpectrumsPlot	
PrepareTrinucleotideSpectrumsTable	
PrintLog	
QueryAnnotatedVCF	
ReadOptimizationIterationReport	
ReadVCF	
PapartEIDEVATP agults	. 47

4 Annotate VCFObj

Anno	rtateVCFObj AnnotateVCFObj	
Index		60
	WriteVCF	59
	WriteFIREVATResultsToTSV	
	UpdateFilter	
	TriNuc.Mutation.Type.Hex.Colors	
	Test.Obj.Fn.2	
	Test.Obj.Fn.1	56
	Sigmoid.Obj.Fn	55
	Sig.Extraction.Obj.Fn	55
	RunMutPat	54
	RunMutaliskHelper	53
	RunMutalisk	52
	RunManualMode	51
	RunGAMode	51
	RunFIREVAT	48

Description

Annotates a vcf.obj using df.variants.of.interest (from PrepareAnnotationDB)

Usage

```
AnnotateVCFObj(vcf.obj, df.annotation.db, columns.to.include,
  include.all.columns = FALSE)
```

Arguments

```
vcf.obj ReadVCF

df.annotation.db

A data.frame from PrepareAnnotationDB. This data.frame must have the columns 'CHROM', 'POS', 'REF', 'ALT'
```

columns.to.include

A character vector of columns to include. Note that existing columns in vcf.obj will not be affected.

include.all.columns

A boolean value. If TRUE, then annotates vcf.obj with all columns present in df.variants.of.interest. If FALSE, columns.to.include must be supplied.

Value

An annotated vcf.obj

CheckIfVariantRefinementIsNecessary

CheckIfVariantRefinementIsNecessary

Description

Checks if variant refinement is necessary by identifying mutational signatures related to sequencing artifact in the vcf.obj (set of original unrefined point mutations).

Usage

```
CheckIfVariantRefinementIsNecessary(vcf.obj, bsg, df.mut.pat.ref.sigs,
  target.mut.sigs, sequencing.artifact.mut.sigs,
  init.artifact.stop = 0.05, verbose = TRUE)
```

Arguments

vcf.obj A list from ReadVCF

bsg BSgenome.Hsapiens.UCSC object

df.mut.pat.ref.sigs

A data.frame from MutPatParseRefMutSigs

target.mut.sigs

A character vector of target mutational signatures from reference mutational signatures.

sequencing.artifact.mut.sigs

A character vector of sequencing artifact mutational signatures from reference mutational signatures.

init.artifact.stop

Numeric value less than 1. If the sum of sequencing artifact weights in vcf.obj is less than or equal to this value then this function returns judgment = FALSE, otherwise returns judgment = TRUE.

verbose

If TRUE, provides process detail. Default value is TRUE.

Value

A list with the following elements

- judgmentA boolean value
- seq.art.sigs.weights.sumA numeric value. Sum of sequencing artifact weights.

6 ComputeZScore

Chromosome.Names

Constant

Description

Chromosome names for FIREVAT. Chromosome names should be given in the format of "chr" + chromosome number.

Usage

Chromosome.Names

Format

An object of class character of length 25.

ComputeZScore

ComputeZScore

Description

Returns a z-score of x given a distribution of values

Usage

```
ComputeZScore(values, x)
```

Arguments

values a numeric vector x a numeric value

Value

a numeric value corresponding to the z-score of x

 ${\tt Compute ZScore EquiValue}$

ComputeZScoreEquiValue

Description

Returns a numeric value that is equivalent to the specified z.score in the distribution of 'values'

Usage

```
ComputeZScoreEquiValue(z.score, values)
```

Arguments

z.score numeric value values numeric vector

Value

a numeric value corresponding to the specified z.score in the 'values' distribution

DecimalCeiling

Decimal Ceiling

Description

Returns the ceiling of a decimal value e.g. value = 0.15, decimal = 0.1 returns 0.2

Usage

```
DecimalCeiling(value, decimal)
```

Arguments

value numeric value (decimal)

decimal numeric value (e.g. 0.1, 0.001)

Value

a numeric value

DefaultFilterToBinary

Default.Obj.Fn Default.Obj.Fn

Description

Calculates the default objective value for FIREVAT GA optimization.

Usage

```
Default.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

DefaultFilterToBinary Transform default filtering parameters to a binary vector

Description

This function transforms default filtering parameter to binary vector which can be used as a suggested solution in GA algorithm.

Usage

```
DefaultFilterToBinary(vcf.filter, params.bit.len)
```

Arguments

```
vcf.filter A list generated in MakeFilter
params.bit.len A list with bit lengths of filtering parameters which is generated from ParameterToBits
```

Value

A binary vector

Enumerate Tri Nuc Counts 9

EnumerateTriNucCounts EnumerateTriNucCounts

Description

Returns C>A, C>G, C>T, T>A, T>C, T>G counts

Usage

EnumerateTriNucCounts(spectrum)

Arguments

spectrum

a numeric vector with 96 numeric values

Details

Please note that this function assumes that 'spectrum' is sorted (i.e. $1:16 \rightarrow C>A$; $17:32 \rightarrow C>G$; $33:48 \rightarrow C>T$; $49:64 \rightarrow T>A$; $65:80 \rightarrow T>C$; $81:96 \rightarrow T>G$)

Value

a numeric vector of length 6 corresponding to the counts of each trinucleotide change (C>A, C>G, C>T, T>A, T>C, T>G)

```
Euc.Exp.Weighted.Obj.Fn
```

Euc.Exp.Weighted.Obj.Fn

Description

Calculates the Euclidean-distance of logarithmically weighted objective value for FIREVAT GA optimization.

Usage

```
Euc.Exp.Weighted.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

```
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.1

Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.1
```

Description

Calculates the Euclidean-distance of logarithmically weighted objective value for FIREVAT GA optimization.

Usage

```
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.1(C.refined, A.refined, C.artifactual,
   A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

```
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.2

Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.2
```

Description

Calculates the Euclidean-distance of logarithmically weighted objective value for FIREVAT GA optimization.

Usage

```
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.2(C.refined, A.refined, C.artifactual,
   A.artifactual)
```

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Euc.Obj.Fn

Value

A numeric value between 0 and 1.

Euc.Obj.Fn

Euc.Obj.Fn

Description

Calculates the Euclidean-distance based objective value for FIREVAT GA optimization.

Usage

```
Euc.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

```
Exp.Weighted.A.Art.Obj.Fn

Exp.Weighted.A.Art.Obj.Fn
```

Description

Exponentially weighted objective function

Usage

```
Exp.Weighted.A.Art.Obj.Fn(C.refined, A.refined, C.artifactual,
   A.artifactual)
```

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

```
\label{eq:continuous} {\it Exp. Weighted. A. Ref. Obj. Fn} \\ {\it Exp. Weighted. A. Ref. Obj. Fn}
```

Description

Exponentially weighted objective function

Usage

```
Exp.Weighted.A.Ref.Obj.Fn(C.refined, A.refined, C.artifactual,
   A.artifactual)
```

Arguments

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

```
{\tt Exp.Weighted.Obj.Fn.1} \ \ \textit{Exp.Weighted.Obj.Fn.1}
```

Description

Calculates the exponentially weighted objective value for FIREVAT GA optimization.

Usage

```
Exp.Weighted.Obj.Fn.1(C.refined, A.refined, C.artifactual, A.artifactual)
```

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

```
Exp.Weighted.Obj.Fn.2 Exp.Weighted.Obj.Fn.2
```

Description

Calculates the exponentially weighted objective value for FIREVAT GA optimization.

Usage

```
Exp.Weighted.Obj.Fn.2(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

```
Exp.Weighted.Refined.Seq.Art.Only.Obj.Fn

Exp.Weighted.Refined.Seq.Art.Only.Obj.Fn
```

Description

Calculates the Euclidean-distance of logarithmically weighted objective value for FIREVAT GA optimization.

Usage

```
Exp.Weighted.Refined.Seq.Art.Only.Obj.Fn(C.refined, A.refined,
   C.artifactual, A.artifactual)
```

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

14 FilterVCF

Value

A numeric value between 0 and 1.

```
FilterByStrandBiasAnalysis
```

Filter By Strand Bias Analysis

Description

Filters refined.vcf.obj by strand bias analysis and moves these filtered variants to artifactual.vcf.obj

Usage

```
FilterByStrandBiasAnalysis(refined.vcf.obj, artifactual.vcf.obj, perform.fdr.correction, filter.by.strand.bias.analysis.cutoff)
```

Arguments

```
refined.vcf.obj

A list of vcf data
artifactual.vcf.obj

A list of vcf data
perform.fdr.correction

A boolean value.
filter.by.strand.bias.analysis.cutoff
A numeric value.
```

Value

A list with filtering parameter values

- refined.vcf.obj updated refined.vcf.obj
- artifactual.vcf.obj updated artifactual.vcf.obj

FilterVCF

FilterVCF

Description

Filter vcf based on the filter Filtering parameters are saved in config.obj Split vcf.obj into vcf.obj.filtered & vcf.obj.artifact based on vcf.filter

Usage

```
FilterVCF(vcf.obj, vcf.filter, config.obj, include.array = NULL,
  force.include = FALSE, verbose = TRUE)
```

GenerateConfigObj 15

Arguments

vcf.obj A list from ReadVCF

vcf.filter A list from MakeMuTect2Filter config.obj A list from ParseConfigFile

include.array A boolean vector

force.include A boolean value. If TRUE, then uses 'include.array'

verbose If true, provides process detail

Value

A list with the following elements

- 1) Mutations which passed filteringvcf.obj.filtered = vcf.obj (list with data, header, genome)
- 2) Mutations which did not pass filteringvcf.obj.artifact = vcf.obj (list with data, header, genome)

GenerateConfigObj Generate config.obj by checking vcf header

Description

This function generate config.obj by checking vcf header. Users should fill in the information needed in console. In current version, only Integers & Float values can be used in config.obj for running FIREVAT.

Usage

```
GenerateConfigObj(vcf.obj, save.config = TRUE,
  config.path = "../temp/FIREVAT_configure.json")
```

Arguments

vcf.obj A list from ReadVCF

save.config If true, save config.obj to config.path

config.path File path to write config.obj (json or yaml)

Value

config.obj

GetCOSMICMutSigs

GetCOSMICMutSigs

Description

Returns a data.frame of the COSMIC mutational signature reference file from the data directory

Usage

GetCOSMICMutSigs()

Value

a data.frame of the COSMIC reference mutational signatures

 $\label{lem:getCOSMICMutSigsEtiologiesColors} Get COSMICMutSigsNames$

Description

Returns all COSMIC mutational signature etiologies and colors

Usage

GetCOSMICMutSigsEtiologiesColors()

Value

data.frame with following columns: signature, group and color.

 ${\tt GetCOSMICMutSigsNames} \quad \textit{GetCOSMICMutSigsNames}$

Description

Returns all COSMIC mutational signature names

Usage

GetCOSMICMutSigsNames()

Value

a character vector

GetGASuggestedSolutions

GetGASuggestedSolutions

Description

Computes suggested solutions

Usage

```
GetGASuggestedSolutions(vcf.obj, bsg, config.obj, lower.upper.list,
   df.mut.pat.ref.sigs, target.mut.sigs, sequencing.artifact.mut.sigs,
   objective.fn, original.muts.seq.art.weights.sum, ga.preemptive.killing,
   verbose = TRUE)
```

Arguments

vcf.obj A list from ReadVCF

bsg BSgenome.Hsapiens.UCSC object

config.obj A list from ParseConfigFile

lower.upper.list

A list from GetParameterLowerUpperVector

df.mut.pat.ref.sigs

A data.frame from MutPatParseRefMutSigs

target.mut.sigs

A character vector of the target mutational signatures from reference mutational signatures.

sequencing.artifact.mut.sigs

A character vector of the sequencing artifact mutational signatures from reference mutational signatures.

objective.fn Objective value derivation function.

original.muts.seq.art.weights.sum

A numeric value. 'seq.art.sigs.weights.sum' from CheckIfVariantRefinementIs-Necessary

ga.preemptive.killing

If TRUE, then preemptively kills populations that yield greater sequencing artifact weights sum compared to the original mutatational signatures analysis

verbose If TRUE, provides process detail. Default value is TRUE.

Value

A list with the following elements

- judgmentA boolean value
- seq.art.sigs.weightsA numeric value. Sum of sequencing artifact weights.

 ${\tt GetOptimizedSignatures}$

GetOptimizedSignatures

Description

This function fetches the last row from the optimization iteration log and returns the target and artifactual mutational signatures for the type of mutations ('refined' or 'artifactual')

Usage

```
GetOptimizedSignatures(data, mutations.type = "refined",
    signatures = "all")
```

Arguments

data A list of main data from RunFIREVAT

mutations.type A string for type of mutations ('refined' or 'artifact')

signatures A string ('all', 'target', 'artifact')

Value

A data.frame with the columns 'signature' and 'weight'

 ${\tt GetParameterLowerUpperVector}$

GetParameterLowerUpperVector

Description

Return a lower/upper vector needed to conduct FIREVAT GA real-valued optimization.

Usage

```
GetParameterLowerUpperVector(vcf.obj, config.obj, vcf.filter,
  multiplier = 100)
```

vcf.obj	A list from ReadVCF
config.obj	A list from ParseConfigFile
vcf.filter	A list from MakeMuTect2Filter
multiplier	A multiplier for convert fraction to integer (default = 100)

GetPCAWGMutSigs 19

Details

vcf.obj\$data: if max(vcf.obj\$data[[param]]) < 1, then multiply multiplier to the vector

Value

A list with the elements

- lower.vector A numeric vector. Each element is the minimum value of each parameter
- upper.vector A numeric vector. Each element is the maximum value of each parameter
- · vcf.obj vcf.obj with updated data

GetPCAWGMutSigs

GetPCAWGMutSigs

Description

Returns the PCAWG mutational signatures data

Usage

```
GetPCAWGMutSigs(sequencing.type = "wes")
```

Arguments

sequencing.type

A string value. It can be either 'wes' for whole-exome sequencing or 'wgs' for whole-genome sequencing

Value

a data.frame of the PCAWG mutatioanl signatures

```
{\tt GetPCAWGMutSigsEtiologiesColors}
```

GetPCAWGMutSigsEtiologiesColors

Description

Returns the PCAWG mutational signatures etiologies and colors

Usage

```
GetPCAWGMutSigsEtiologiesColors()
```

Value

```
a data.frame with the columns 'signature', 'group', 'color'
```

 ${\tt GetPCAWGMutSigsNames} \quad \textit{GetPCAWGMutSigsNames}$

Description

Returns the PCAWG mutational signatures names

Usage

GetPCAWGMutSigsNames()

Value

a character vector of the PCAWG mutational signatures names

GetPCAWGPlatinumMutSigs

GetPCAWGPlatinumMutSigs

Description

Returns the PCAWG platinum mutational signatures data

Usage

GetPCAWGPlatinumMutSigs()

Value

a data.frame of the PCAWG platinum mutatioanl signatures

 $\label{lem:GetPCAWGPlatinumMutSigsEtiologiesColors} GetPCAWGPlatinumMutSigsEtiologiesColors$

Description

Returns the PCAWG platinum mutational signatures etiologies and colors

Usage

GetPCAWGPlatinumMutSigsEtiologiesColors()

Value

a data.frame with the columns 'signature', 'group', 'color'

 ${\tt GetPCAWGPlatinumMutSigsNames}$

GetPCAWGPlatinumMutSigsNames

Description

Returns the PCAWG platinum mutational signatures names

Usage

```
GetPCAWGPlatinumMutSigsNames()
```

Value

a character vector of the PCAWG platinum mutational signatures names

GetSeedForVCF

GetSeedForVCF

Description

Returns a seed integer based on VCF file size

Usage

```
GetSeedForVCF(vcf.file)
```

Arguments

```
vcf.file (full path of a .vcf file)
```

Details

Returns the same seed integer for the same VCF file (based on file size)

Value

an integer value

InitializeVCF	InitializeVCF

Description

Initialize VCF with FIREVAT config file This functions selects point mutations and appends filter values to vcf.obj\$data

Usage

```
InitializeVCF(vcf.obj, config.obj, verbose = TRUE)
```

Arguments

vcf.obj A list from ReadVCF
config.obj A list from ParseConfigFile
verbose If true, provides process detail

Value

A list with the following elements

- vcf.obj.filteredvcf.obj (high-quality vcf)
- vcf.obj.artifactvcf.obj (low-quality vcf)

```
Leaky.ReLU.A.Art.Obj.Fn

Leaky.ReLU.A.Art.Obj.Fn
```

Description

Leaky ReLU objective function

Usage

```
Leaky.ReLU.A.Art.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

 $\begin{array}{lll} \hbox{C.refined} & A \text{ numeric value between 0 and 1.} \\ \hbox{A.refined} & A \text{ numeric value between 0 and 1.} \\ \hbox{C.artifactual} & A \text{ numeric value between 0 and 1.} \\ \hbox{A.artifactual} & A \text{ numeric value between 0 and 1.} \\ \end{array}$

Value

A numeric value between 0 and 1.

```
Leaky.ReLU.A.Ref.Obj.Fn
```

Leaky.ReLU.A.Ref.Obj.Fn

Description

Leaky ReLU objective function

Usage

```
Leaky.ReLU.A.Ref.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined	A numeric value between 0 and 1.
A.refined	A numeric value between 0 and 1.
C.artifactual	A numeric value between 0 and 1.
A.artifactual	A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

```
Leaky.ReLU.Obj.Fn Leaky.ReLU.Obj.Fn
```

Description

Lkeay ReLU objective function

Usage

```
Leaky.ReLU.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

MakeFilter

MakeFilter

Description

Creates a vcf filter from config.obj

Usage

```
MakeFilter(config.obj)
```

Arguments

config.obj

A list from ParseConfigFile (any filter with "use_in_filter" value declared as FALSE is not considered)

Value

A list with the filter parameters

MutaliskParseVCF0bj

MutaliskParseVCFObj

Description

Parses a vcf.obj and prepares it to run Mutalisk.

Usage

```
MutaliskParseVCFObj(vcf.obj)
```

Arguments

vcf.obj

A list from ReadVCF

Value

A data.frame

MutPatParseRefMutSigs MutPatParseRefMutSigs

Description

Parses a df.ref.mut.sigs and prepares it to run Mutational Patterns.

Usage

```
MutPatParseRefMutSigs(df.ref.mut.sigs, target.mut.sigs,
    signature.start.column.index = 4,
    mutation.type.header = "SomaticMutationType")
```

Arguments

```
df.ref.mut.sigs
A data.frame of reference mutational signatures

target.mut.sigs
A character vector of target mutational signatures names

signature.start.column.index
= An integer value (e.g. column index corresponding to 'SBS1')

mutation.type.header
= A string value (name of header corresponding to column containing 'A[C>A]A' data))
```

Value

A data.frame of the format deconstructSigs::signatures.cosmic

MutPatParseVCFObj MutPatParseVCFObj

Description

Parses a vcf.obj and prepares it to run Mutational Patterns.

Usage

```
MutPatParseVCFObj(vcf.obj, bsg, sample.id = "sample")
```

Arguments

vcf.obj A list from ReadVCF

bsg BSgenome.Hsapiens.UCSC.hg19::BSgenome.Hsapiens.UCSC.hg19 or BSgenome.Hsapiens.UCSC.hg38

sample.id A string value

26 ParseConfigFile

Value

A data frame with the column sample id and row names corresponding to 96 substitution types

neterToBits

Description

Calculate the number of bits needed to conduct FIREVAT GA binary optimization.

Usage

```
ParameterToBits(vcf.obj, config.obj, vcf.filter, multiplier = 100)
```

Arguments

vcf.obj	A list from ReadVCF
config.obj	A list from ParseConfigFile
vcf.filter	A list from MakeMuTect2Filter
multiplier	A multiplier for convert fraction to integer (default = 100)

Details

vcf.obj\$data: if max(vcf.obj\$data[[param]]) < 1, then multiply multiplier to the vector

Value

A list with the elements

- params.bit.lenA numeric vector. Each element is the bit length of each parameter value
- vcf.objA vcf.obj (ReadVCF) with updated data

Description

This function returns config.obj from JSON or YAML config file. - Check if the config file is in JSON format or YAML format - Return config.obj

Usage

```
ParseConfigFile(config.path, verbose = TRUE)
```

Arguments

config.path A string for config file path verbose If true, provides process detail

Value

```
config.obj: list of parameters
```

Examples

```
## Not run:
ParseConfigFile("example.variant.caller.json")
ParseConfigFile("example.variant.caller.json", verbose=False)
## End(Not run)
```

```
PCAWG.All.Sequencing.Artifact.Signatures

**Constant**
```

Description

PCAWG mutational signatures reported to be associated with sequencing artifacts

Usage

```
PCAWG.All.Sequencing.Artifact.Signatures
```

Format

An object of class character of length 18.

```
{\it PCAWG.} Known. Sequencing. Artifact. Signatures \\ {\it Constant}
```

Description

PCAWG mutational signatures reported to be associated with sequencing artifacts

Usage

```
PCAWG.Known.Sequencing.Artifact.Signatures
```

Format

An object of class character of length 1.

PCAWG.Platinum.All.Technology.Related.Artifact.Signatures

Constant

Description

PCAWG mutational signatures reported to be associated with sequencing artifacts

Usage

PCAWG.Platinum.All.Technology.Related.Artifact.Signatures

Format

An object of class character of length 9.

PCAWG.Possible.Sequencing.Artifact.Signatures

Constant

Description

PCAWG mutational signatures reported to be associated with sequencing artifacts

Usage

PCAWG.Possible.Sequencing.Artifact.Signatures

Format

An object of class character of length 17.

PCAWG.Target.Mutational.Signatures

Constant

Description

PCAWG target mutational signatures reported to be unrelated to sequencing artifacts

Usage

PCAWG.Target.Mutational.Signatures

Format

An object of class character of length 47.

PerformStrandBiasAnalysis

PerformStrandBiasAnalysis

Description

Performs strand bias analysis

Usage

```
PerformStrandBiasAnalysis(vcf.obj, ref.forward.strand.var,
  ref.reverse.strand.var, alt.forward.strand.var, alt.reverse.strand.var,
  perform.fdr.correction = TRUE, fdr.correction.method = "BH")
```

Arguments

Value

An updated vcf.obj

PlotMutaliskResults PlotMutaliskResults

Description

Plots Mutalisk results

Usage

```
PlotMutaliskResults(mutalisk.results, signatures,
  df.ref.sigs.groups.colors, trinuc.max.y, trinuc.min.y, mut.type.max.y,
  title, font.size.small = 8, font.size.med = 14)
```

30 PlotMutationTypes

Arguments

```
mutalisk.results
                 A list obtained from RunMutalisk
signatures
                 A character vector of mutational signatures names
df.ref.sigs.groups.colors
                 A data.frame with signature groups and colors
                 A numeric value (maximum y-axis value)
trinuc.max.y
trinuc.min.y
                 A numeric value (minimum y-axis value)
mut.type.max.y A numeric value
title
                 A string value
font.size.small
                 A numeric value
font.size.med
               A numeric value
```

Value

A ggplot object

Examples

 ${\tt PlotMutationTypes}$

PlotMutationTypes

Description

Plots a horizontal barplot of mutation types

Usage

```
PlotMutationTypes(mutation.types = c("C>A", "C>G", "C>T", "T>A", "T>C", "T>G"), mutation.types.values, mutation.types.colors, max.y.val, title, convert.to.percentage = T, show.legend = T, font.size.small = 8, font.size.med = 14, plot.margin = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
```

Arguments

```
mutation.types \;\; Mutation \; types; \; Default = c("C>A", "C>G", "C>T", "T>A", "T>C", "T>G")
mutation.types.values
                  Mutation count for each mutation type
mutation.types.colors
                  A color vector for indicating mutation types
max.y.val
                  y axis maximum value
title
                  Plot title
convert.to.percentage
                  if True convert y values to percentage (x 100); Default = T
show.legend
                  If True, show legend; Default = T
font.size.small
                  Small font size; Default = 8
font.size.med
                  Medium font size; Default = 14
                  Margin vector for drawing plot; Default = unit(c(0.5, 0.5, 0.5, 0.5, 0.5), "cm"))
plot.margin
```

Value

A ggplot object

Examples

PlotOptimizationIterations

PlotOptimizationIterations

Description

Plots multiple scatter plots into one figure

Usage

```
PlotOptimizationIterations(df, columns.to.plot, x.axis.var, x.axis.title,
    x.min, x.max, save.file, title, y.axis.title = "", y.max = 1,
    point.size = 1, connect.dots = T, plot.legend = T,
    legend.ncol = 1, font.size.med = 14, font.size.large = 16,
    plot.margin = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
```

Arguments

```
A data.frame (from reading "FIREVAT_Optimization_Logs.tsv")
df
columns.to.plot
                  A character vector (of column names to plot)
x.axis.var
                  x axis variable
x.axis.title
                  x axis title
                  x axis maximum value
x.max
save.file
                  Filename (including full path) to which the plot will be saved
title
                  Plot title
                  y axis title; Default = ""
y.axis.title
y.max
                  y axis maximum value; Default = 1
                  Point size; Default = 1
point.size
connect.dots
                  If True draws dots for each iteration; Default = True
plot.legend
                  If True write legend of plot; Default = T
legend.ncol
                  legend.n Default = 1
font.size.med
                  Medium font size; Default = 14
font.size.large
                  Large font size; Default = 16
                  Margin vector for plot; Default = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
plot.margin
```

Value

A ggplot object

PlotSignaturesContProbs

PlotSignaturesContProbs

Description

Plots a horizontal barplot of identified mutational signatures

PlotTable 33

Usage

```
PlotSignaturesContProbs(df.identified.mut.sigs, df.ref.sigs.groups.colors,
  title, convert.to.percentage = T, font.size.small = 8,
  font.size.med = 14, plot.margin = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
```

Arguments

```
df.identified.mut.sigs
A data.frame of identified mutational signatures

df.ref.sigs.groups.colors
A data.frame with 'signature', 'group', and 'color' columns

title
Plot title
convert.to.percentage
If true, convert y values to percentage (x 100); Default = T,

font.size.small
Small font size; Default = 8,

font.size.med
Medium font size; Default = 14,

plot.margin
Margin vector for drawing plot; Default = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
```

Value

A ggplot object

Examples

```
## Not run:
    g <- PlotSignaturesContProbs(sigs = c(mutalisk.results$identified.mut.sigs),
    sigs.probs = c(mutalisk.results$identified.mut.sigs.probs),
    df.ref.sigs.groups.colors = GetPCAWGMutSigsEtiologiesColors())
    print(g)
## End(Not run)</pre>
```

PlotTable

PlotTable

Description

Plots basic statistics table

Usage

```
PlotTable(df, padding = 20, font.size = 14)
```

PlotTriNucSpectrum

Arguments

34

df = A data.frame where the first column is header and the second column is data

value

padding Padding size; Default = 20 font.size Font size; Default = 14

Value

A plot

PlotTriNucSpectrum PlotTriNucSpectrum

Description

Plots the spectrum of 96 trinucleotide distribution (C>A, C>G, C>T, T>A, T>C, T>G) Please note that this function assumes that both sub.types and spectrum are sorted in the following order: C>A, C>G, C>T, T>A, T>C, T>G

Usage

```
PlotTriNucSpectrum(sub.types, spectrum, max.y.val, min.y.val, y.axis.title,
  draw.top.strip = T, draw.x.axis.labels = T, draw.y.axis.labels = T,
  draw.y.axis.title = T, font.size.small = 8, font.size.med = 14,
  plot.margin.top = 0.5, plot.margin.bottom = 0.5,
  plot.margin.left = 0.5, plot.margin.right = 0.5, title)
```

Arguments

font.size.med

```
A character vector (types of 96 trinucleotide substitutions)
sub.types
                  A numeric vector (96 elements)
spectrum
max.y.val
                  y axis maximum value
min.y.val
                  y axis minimum value
y.axis.title
                  y axis title
draw.top.strip If True then draws top strip; Default = T
draw.x.axis.labels
                  If True then draws x axis labels; Default = T
draw.y.axis.labels
                  If True then draws y axis labels; Default = T
draw.y.axis.title
                  If True then draws y axis title; Default = T
font.size.small
                  Small font size; Default = 8
```

Medium font size; Default = 14

PlotVCFStatsBoxPlots 35

```
Top margin; Default = 0.5

plot.margin.bottom

Bottom margin; Default = 0.5

plot.margin.left

Left margin; Default = 0.5

plot.margin.right

Right margin; Default = 0.5

title Plot title
```

Value

A ggplot object

PlotVCFStatsBoxPlots PlotVCFStatsBoxPlots

Description

Plots multiple (original, refined, artifact vcf) boxplots for single filter parameter

Usage

```
PlotVCFStatsBoxPlots(original.vcf.stat.values, refined.vcf.stat.values,
  artifact.vcf.stat.values, xlab, axis.font.size = 10,
  label.font.size = 10, title.font.size = 12)
```

Arguments

```
original.vcf.stat.values
```

A numeric vector corresponding to the original vcf.obj values of single filter parameter

refined.vcf.stat.values

A numeric vector corresponding to the refined vcf.obj values of single filter parameter

artifact.vcf.stat.values

A numeric vector corresponding to the artifact vcf.obj values of single filter parameter

xlab A string value (x-axis label)

axis.font.size An integer value (axis font size)

label.font.size

An integer value (label font size)

title.font.size

An integer value (title font size)

Value

A ggboxplot

PlotVCFStatsHistograms

PlotVCFStatsHistograms

Description

Plots multiple VCF stats histograms into one figure

Usage

```
PlotVCFStatsHistograms(plot.values, x.axis.labels, stat.y.max.vals,
   stat.x.max.vals, sample.id, save.file, title, cutoff.values,
   plot.boxplot = F, plot.cutoff.line.color = "#D4012E",
   plot.cutoff.value.lines = F, bin.width = 1, ncol = 4, nrow = 3,
   font.size.med = 10, font.size.large = 12, plot.margin = unit(c(0.5,
   0.5, 0.5, 0.5), "cm"))
```

```
plot.values
                  A list of multiple numeric vectors
x.axis.labels
                  A character vector of x axis labels
stat.y.max.vals
                  A numeric vector of max y-axis values
stat.x.max.vals
                  A numeric vector of max x-axis values
sample.id
                  A string value of sample ID
save.file
                  A string value of file to which the resulting plot will be saved
title
                  A string value of plot title
cutoff.values
                  A numeric vector of cutoff values
plot.boxplot
                  A boolean value (default = False)
plot.cutoff.line.color
                  A hex string value (default = "#D4012E")
plot.cutoff.value.lines
                  A boolean value (default = False)
bin.width
                  An integer value (default = 1; histogram bin width)
ncol
                  An integer value (default = 4; ggarrange ncol)
                  An integer value (default = 3; ggarrange nrow)
nrow
font.size.med
                  An integer value (default = 10)
font.size.large
                  An integer value (default = 12)
                  A list (default = unit(c(0.5, 0.5, 0.5, 0.5), "cm"))
plot.margin
```

PrepareAnnotationDB 37

Value

A list with the following elements

- f = A ggarrange object
- graphs = A list of length 3; each element is a ggplot histogram

PrepareAnnotationDB

Prepare Annotation DB

Description

Prepares df.genes.of.interest from a vcf.obj (ReadVCF) of COSMIC or ClinVar vcf for AnnotateVCFObj

Usage

PrepareAnnotationDB(annotation.vcf.obj)

Arguments

```
annotation.vcf.obj vcf.obj of COSMIC or ClinVar vcf file
```

Value

A data.frame of annotation.vcf.obj

 ${\tt Prepare Artifact Annotation Table}$

Prepare Artifact Annotation Table

Description

Prepares artifactual mutations annotation (filtered, queried) table

Usage

PrepareArtifactAnnotationTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 ${\tt PrepareArtifactStrandBiasTable}$

Prepare Artifact Strand Bias Table

Description

Prepares artifactual mutations strand biased variants table

Usage

PrepareArtifactStrandBiasTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 $\label{lem:prepareArtifactualMutsOptimizationIterationsPlot} PrepareArtifactualMutsOptimizationIterationsPlot$

Description

Prepares artifactual mutations optimization iterations plot

Usage

PrepareArtifactualMutsOptimizationIterationsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A ggplot object

 ${\tt PrepareFilterCutoffsTable}$

Prepare Filter Cutoffs Table

Description

Prepares filter cutoffs table for reporting

Usage

PrepareFilterCutoffsTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 ${\tt Prepare Genetic Algorithm Parameters Table}$

Prepare Genetic Algorithm Parameters Table

Description

Prepares Genetic Algorithm parameters table

Usage

 ${\tt Prepare Genetic Algorithm Parameters Table (data)}$

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 ${\tt PrepareIdentifiedSignaturesPlot}$

Prepare Identified Signatures Plot

Description

Prepares identified signatures plot for reporting

Usage

PrepareIdentifiedSignaturesPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A ggarrange object

 ${\tt Prepare MLERe constructed Spectrums Plot}$

Prepare MLE Reconstructed Spectrums Plot

Description

Prepares MLE reconstructed spectrums plot

Usage

PrepareMLEReconstructedSpectrumsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

 ${\tt Prepare Nucleotide Substitution Types Plot}$

Prepare Nucleotide Substitution Types Plot

Description

Prepares nucleotide substitution types plot

Usage

PrepareNucleotideSubstitutionTypesPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A ggarrange object

 ${\tt Prepare Observed Spectrums Plot}$

PrepareObservedSpectrumsPlot

Description

Prepares observed spectrums plot

Usage

PrepareObservedSpectrumsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

PrepareOptimizationResultsTable

 ${\it Prepare Optimization Results Table}$

Description

Prepares optimization results table

Usage

PrepareOptimizationResultsTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

PrepareOptimizedVCFStatisticsPlot

Prepare Optimized VCF Statistics Plot

Description

Prepares optimized VCF statistics plot

Usage

PrepareOptimizedVCFStatisticsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

 ${\tt Prepare Refined Annotation Table}$

Prepare Refined Annotation Table

Description

Prepares refined mutations annotation (filtered, queried) table

Usage

PrepareRefinedAnnotationTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 ${\tt Prepare Refined Muts Optimization Iterations Plot}$

Prepare Refined Muts Optimization Iterations Plot

Description

Prepares refined mutations optimization iterations plot

Usage

PrepareRefinedMutsOptimizationIterationsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A ggplot object

 ${\tt Prepare Refined Strand Bias Table}$

 ${\it Prepare Refined Strand Bias Table}$

Description

Prepares refined mutations strand biased variants table

Usage

PrepareRefinedStrandBiasTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

 ${\tt PrepareResidualSpectrumsPlot}$

PrepareResidualSpectrumsPlot

Description

Prepares residual spectrums plot

Usage

PrepareResidualSpectrumsPlot(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

 ${\tt PrepareTrinucleotideSpectrumsTable}$

Prepare Trinucle ot ide Spectrums Table

Description

Prepares trinucleotide spectrums table

Usage

PrepareTrinucleotideSpectrumsTable(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame

PrintLog

PrintLog

Description

Prints log message

Usage

```
PrintLog(msg, type = "INFO")
```

Arguments

msg String value message to print along with log type and date

type String value that represents type of this message. 'INFO' by default.

 ${\tt QueryAnnotatedVCF}$

FilterAnnotatedVCF

Description

Annotates a vcf.obj using df.variants.of.interest (from (PrepareAnnotationDB)

Usage

```
QueryAnnotatedVCF(vcf.obj.annotated, filter.key.value.pairs,
  filter.condition = "AND")
```

Arguments

```
vcf.obj.annotated
```

AnnotateVCF0bj

filter.key.value.pairs

A list with the key as the column name and value as the filtering values. E.g. list("CLNSIG" = c("Pathogenic", "Pathogenic/Likely_pathogenic"))

filter.condition

'AND' or 'OR'.

Value

A vcf.obj

 ${\tt ReadOptimizationIterationReport}$

ReadOptimizationIterationReport

Description

Read optimization iteration report

Usage

ReadOptimizationIterationReport(data)

Arguments

data

A list of elements returned from RunFIREVAT

Value

A data.frame of FIREVAT optimization logs

ReadVCF 47

ReadVCF

ReadVCF

Description

Reads a .vcf file

Usage

```
ReadVCF(vcf.file, genome = "hg19", split.info = FALSE,
   check.chromosome.name = TRUE)
```

Arguments

vcf.file (full path of a .vcf file) genome ('hg19' or 'hg38')

split.info A boolean value. If TRUE, then makes the INFO column in the vcf as a separate

column. Default value is FALSE.

check.chromosome.name

A boolean value. If TRUE, then check whether converts 'MT' to 'M' and adds

'chr' to the CHROM column. Default value is TRUE.

Value

A list with elements 'data', 'header', 'genome'

```
ReportFIREVATResults ReportFIREVATResults
```

Description

Reports FIREVAT results in html format (generated from Rmd)

Usage

```
ReportFIREVATResults(data)
```

Arguments

data

A list of main data from RunFIREVAT

Value

An updated data list

48 RunFIREVAT

RunFIREVAT

RunFIREVAT

Description

Runs FIREVAT using configuration data. Filters point mutations in the user-specified vcf file based on mutational signature identification and outputs the refined and artifact vcf files as well as metadata related to the refinement process.

Usage

```
RunFIREVAT(vcf.file, vcf.file.genome = "hg19", config.file,
 df.ref.mut.sigs = GetPCAWGMutSigs(),
 target.mut.sigs = GetPCAWGMutSigsNames(),
 df.ref.mut.sigs.groups.colors = GetPCAWGMutSigsEtiologiesColors(),
 sequencing.artifact.mut.sigs = PCAWG.All.Sequencing.Artifact.Signatures,
 num.cores = 2, output.dir, mode = "ga", init.artifact.stop = 0.05,
 objective.fn = Default.Obj.Fn, use.suggested.soln = TRUE,
 ga.type = "real-valued", ga.pop.size = 100, ga.max.iter = 100,
 ga.run = 50, ga.pmutation = 0.1, ga.preemptive.killing = FALSE,
 ga.seed = NULL, mutalisk = TRUE, mutalisk.method = "all",
 mutalisk.must.include.sigs = NULL,
 mutalisk.random.sampling.count = 20,
 mutalisk.random.sampling.max.iter = 10,
 perform.strand.bias.analysis = FALSE,
 filter.by.strand.bias.analysis = TRUE,
 filter.by.strand.bias.analysis.cutoff = 0.25,
 strand.bias.perform.fdr.correction = TRUE,
 strand.bias.fdr.correction.method = "BH",
 ref.forward.strand.var = NULL, ref.reverse.strand.var = NULL,
 alt.forward.strand.var = NULL, alt.reverse.strand.var = NULL,
 annotate = FALSE, df.annotation.db = NULL,
 annotated.columns.to.display = NULL,
 annotation.filter.key.value.pairs = NULL,
 annotation.filter.condition = "AND", write.vcf = TRUE,
 report = TRUE, save.rdata = TRUE, save.tsv = TRUE,
 report.format = "html", verbose = TRUE)
```

Arguments

```
vcf.file String value corresponding to input .vcf file. Please provide the full path.

vcf.file.genome

Genome assembly of the input .vcf file. The value should be eitehr 'hg19' or 'hg38'.

config.file String value corresponding to input configuration file. For more details please refer to ...
```

RunFIREVAT 49

df.ref.mut.sigs

A data frame of the reference mutational signatures

target.mut.sigs

A character vector of the target mutational signatures from reference mutational signatures.

df.ref.mut.sigs.groups.colors

A data frame of the reference mutational signatures groups and colors

sequencing.artifact.mut.sigs

A character vector of the sequencing artifact mutational signatures from reference mutational signatures.

num. cores Number of cores to allocate

output.dir String value of the desired output directory

mode String value. The value should be either 'ga' or 'manual'.

init.artifact.stop

Numeric value less than 1. If the sum of sequencing artifact weights in the user-specified original VCF file (i.e. vcf.file) is less than or equal to this value then FIREVAT does not perform variant refinement. Default value is 0.05. Note that this option does not apply if 'mode' is 'manual'.

objective.fn Objective value derivation function. Default: Default.Obj.Fn.

use.suggested.soln

Boolean value. If TRUE, then FIREVAT passes the default values of filter variables declared as 'use_in_filter' in the config file to the 'suggestions' parameter of the Genetic Algorithm package. If FALSE, then FIREVAT supplies NULL to the GA package 'suggestions' parameter. FIREVAT also computes baseline performance of each filter variable and uses fittest population from each variable as a suggested solution.

ga. type String value. The value should be either 'binray' or 'real-valued'.

ga.pop.size Integer value of the Genetic Algorithm 'population size' parameter. Default: 100. This value should be set based on the number of filter parameters. Recommendation: 40 per filter parameter.

ga.max.iter Integer value of the Genetic Algorithm 'maximum iterations' parameter. Default: 100. This value should be set based on the number of filter parameters. Recommendation: same as 'ga.pop.size'.

ga.run Integer value of the Genetic Algorithm 'run' parameter. Default: 50. This value should be set based on the 'ga.max.iter' parameter. Recommendation: 25 percent of 'ga.max.iter'.

ga.pmutation Float value of the Genetic Algorithm 'mutation probability' parameter. Default: 0.1.

ga.preemptive.killing

If TRUE, then preemptively kills populations that yield greater sequencing artifact weights sum compared to the original mutatational signatures analysis

ga. seed Integer value of the Genetic Algorithm 'seed' parameter. Default: NULL.

mutalisk If TRUE, confirm mutational signature analysis with Mutalisk. Default: TRUE.

50 RunFIREVAT

mutalisk.method

Mutalisk signature identification method. Default: 'random.sampling'. The value can be either 'all' or 'random.sampling'. 'all' uses all target.mut.sigs to identify mutational signatures. 'random.sampling' randomly samples from target.mut.sigs to identify mutational signatures.

mutalisk.must.include.sigs

Signatures that must be included in the Mutalisk signature identification A character vector corresponding to the signature names.

mutalisk.random.sampling.count

Mutalisk random sampling count. Default: 20. The number of signatures to sample from target.mut.sigs

mutalisk.random.sampling.max.iter

Mutalisk random sampling maximum iteration. Default: 10. The number of times Mutalisk randomly samples from target.mut.sigs before determining the candidate signatures.

perform.strand.bias.analysis

If TRUE, then performs strand bias analysis.

filter.by.strand.bias.analysis

If TRUE, then filters out variants in refined vcf based on strand bias analysis results

filter.by.strand.bias.analysis.cutoff

The p.value or q value cutoff for filtering out variants.

strand.bias.perform.fdr.correction

If TRUE, then performs false discovery rate correction for strand bias analysis.

strand.bias.fdr.correction.method

A string value. Default value is 'BH'. Refer to 'p.adjust()' function method.

ref.forward.strand.var

A string value.

ref.reverse.strand.var

A string value,

alt.forward.strand.var

A string value,

alt.reverse.strand.var

A string value,

annotate A boolean value. Default value is TRUE.

df.annotation.db

A data.frame. Please refer to PrepareAnnotationDB

annotated.columns.to.display

A character vector.

annotation.filter.key.value.pairs

A list.

annotation.filter.condition

'AND' or 'OR'.

write.vcf If TRUE, write original/refined/artifact vcfs. Default: TRUE.

report If TRUE, generate report. Default: TRUE.

RunGAMode 51

save.rdata If TRUE, save rdata. Default: TRUE. save.tsv If TRUE, save tsv. Default: TRUE.

report. format The format of FIREVAT report. We currently only support 'html'.

verbose If TRUE, provides process detail. Default: TRUE.

Value

A list with the following elements

- f = A ggarrange object
- graphs = A list of length 3; each element is a ggplot histogram

RunGAMode

RunGAMode

Description

Runs FIREVAT ga mode

Usage

RunGAMode(data)

Arguments

data

A list from RunFIREVAT

Value

A list

RunManualMode

RunManualMode

Description

Runs FIREVAT manual mode

Usage

RunManualMode(data)

Arguments

data

A list from RunFIREVAT

Value

A list

52 RunMutalisk

RunMuta]	lick	

RunMutalisk

Description

Identifies mutational signatures using Mutalisk

Usage

```
RunMutalisk(vcf.obj, df.ref.mut.sigs, target.mut.sigs,
  random.sampling.candidate.mut.sigs = c(), method = "random.sampling",
  n.sample = 20, n.iter = 10, verbose = TRUE)
```

Arguments

```
A list (from firevat_vcf::ReadVCF)
vcf.obi
df.ref.mut.sigs
                  A data.frame of reference mutational signatures
target.mut.sigs
                  A character vector of target mutational signatures names to identify from
random.sampling.candidate.mut.sigs
                  A character vector of mutational signatures names that gets appended to the list
                  of candidate mutational signatures so that these are always considered.
method
                  A string value (must be either 'random.sampling' or 'all'). The method 'ran-
                  dom.sampling' samples (without replacement) 'n.sample' number of signatures
                  'n.iter' number of times and runs the candidate signatures one last time. The
                  method 'all' uses all target.mut.sigs
                  An integer value ('random.sampling' method parameter) Number of signatures
n.sample
                  to choose for each iteration of random sampling).
n.iter
                  An integer value ('random.sampling' method parameter). Number of iterations
                  to perform random sampling.
                  If true, provides process details
verbose
```

Value

A list with the following elements

- num.point.mutationsAn integer value count of total point mutations
- sub.typesA character vector of length 96
- sub.types.spectrumA numeric vector of length 96
- num.mut.sigsAn integer value (count of unique mutational signatures identified)
- · identified.mut.sigsA character vector where each element is a mutational signature identified
- identified.mut.sigs.probsA numeric vector where each element is the weight of mutational signature identified. The ordering follows identified.mut.sigs

RunMutaliskHelper 53

- identified.mut.sigs.spectrumA numeric vector of length 96
- residualsA numeric vector of length 96
- rssA numeric value (residual sum of squares)
- cos.sim.scoreA numeric value (cosine similarity score between observed mutational spectrum and reconstructed mutational signatures)
- all.models.sigsA list where each element is a model; a model is a list of signatures identified)
- all.models.sigs.probsA list where each element is a model; a model is a list of contribution probabilities
- all.models.cos.sim.scoresA list where each element is a model; a model is a list of cosine similarity socres

RunMutaliskHelper

RunMutaliskHelper

Description

Helper function for RunMutalisk

Usage

```
RunMutaliskHelper(vcf.trinucleotide.data, df.ref.mut.sigs, target.mut.sigs)
```

Arguments

```
vcf.trinucleotide.data
A data.frame (from firevat_mutalisk::MutaliskParseVCFObj)

df.ref.mut.sigs
A data.frame of reference mutational signatures

target.mut.sigs
A character vector of target mutational signatures names
```

Value

A list with the following elements

- num.point.mutationsAn integer value count of total point mutations
- sub.typesA character vector of length 96
- sub.types.spectrumA numeric vector of length 96
- num.mut.sigsAn integer value (count of unique mutational signatures identified)
- · identified.mut.sigsA character vector where each element is a mutational signature identified
- identified.mut.sigs.probsA numeric vector where each element is the weight of mutational signature identified. The ordering follows identified.mut.sigs
- identified.mut.sigs.spectrumA numeric vector of length 96

54 RunMutPat

- · residualsA numeric vector of length 96
- rssA numeric value (residual sum of squares)
- cos.sim.scoreA numeric value (cosine similarity score between observed mutational spectrum and reconstructed mutational signatures)
- all.models.sigsA list where each element is a model; a model is a list of signatures identified)
- all.models.sigs.probsA list where each element is a model; a model is a list of contribution probabilities
- all.models.cos.sim.scoresA list where each element is a model; a model is a list of cosine similarity socres

RunMutPat

RunMutPat

Description

Identifies mutational signatures using Mutational Patterns

Usage

```
RunMutPat(mut.pat.input, df.mut.pat.ref.sigs, target.mut.sigs,
  verbose = TRUE)
```

Arguments

Value

A list with the following elements

- tumor.mutation.types.spectrumA numeric vector of length 96 'observed' spectrum
- identified.mutation.types.spectrumA numeric vector of length 96 'identified' spectrum
- residuals A numeric vector of length 96 residuals
- mutation.typesA character vector of length 96
- · identified.mut.sigsA character vector where each element is a mutational signature identified
- identified.mut.sigs.contribution.weightsA numeric vector where each element is the weight of mutational signature identified. The ordering follows identified.mut.sigs
- · cosine.similarity.scoreA numeric value

Sig.Extraction.Obj.Fn 55

Examples

```
## Not run:
vcf.obj <- ReadVCF(vcf.file = "../data/sample/HNT-082-BT.final.call.vcf", genome = "hg19")
df.ref.mut.sigs <- GetPCAWGMutSigs()
target.mut.sigs <- GetPCAWGMutSigsNames()
RunMutPat(vcf.obj = vcf.obj,
df.ref.mut.sigs = df.ref.mut.sigs,
target.mut.sigs = target.mut.sigs)
## End(Not run)</pre>
```

```
Sig.Extraction.Obj.Fn Sig.Extraction.Obj.Fn
```

Description

Calculates the default objective value for FIREVAT GA optimization.

Usage

```
Sig.Extraction.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

```
C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.
```

Value

A numeric value between 0 and 1.

```
Sigmoid.Obj.Fn Sigmoid.Obj.Fn
```

Description

Sigmoid objective function

Usage

```
Sigmoid.Obj.Fn(C.refined, A.refined, C.artifactual, A.artifactual)
```

56 Test.Obj.Fn.1

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

Test.Obj.Fn.1 Test.Obj.Fn.1

Description

Test objective function 1

Usage

```
Test.Obj.Fn.1(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

Test.Obj.Fn.2 57

Test.Obj.Fn.2

Test.Obj.Fn.2

Description

Test objective function 2

Usage

```
Test.Obj.Fn.2(C.refined, A.refined, C.artifactual, A.artifactual)
```

Arguments

C.refined A numeric value between 0 and 1.

A.refined A numeric value between 0 and 1.

C.artifactual A numeric value between 0 and 1.

A.artifactual A numeric value between 0 and 1.

Value

A numeric value between 0 and 1.

```
TriNuc.Mutation.Type.Hex.Colors

**Constant**
```

Description

Hex codes for the mutation types (for plotting purposes)

Usage

```
TriNuc.Mutation.Type.Hex.Colors
```

Format

An object of class character of length 6.

UpdateFilter

UpdateFilter

Description

Update filter based on optim parameter values

Usage

```
UpdateFilter(vcf.filter, param.values)
```

Arguments

vcf.filter

A list from MakeFilterFromConfig

param.values

A numeric vector contains filtering value (same length with length(vcf.config.filter))

Value

Updated vcf.filter (list)

WriteFIREVATResultsToTSV

WriteFIREVATResultsToTSV

Description

Writes FIREVAT results to a csv file

Usage

WriteFIREVATResultsToTSV(firevat.results)

Arguments

firevat.results

List returned from RunFIREVAT

Write VCF 59

WriteVCF WriteVCF

Description

Writes a vcf.obj to a .vcf file

Usage

```
WriteVCF(vcf.obj, save.file)
```

Arguments

vcf.obj (from the function ReadVCF) save.file (full path including filename)

Index

```
*Topic datasets
                                                                                                                                                     FilterVCF, 14
             Chromosome. Names, 6
             PCAWG.All.Sequencing.Artifact.Signatures, GenerateConfigObj, 15
                                                                                                                                                      GetCOSMICMutSigs, 16
             PCAWG.Known.Sequencing.Artifact.Signature § tCOSMICMutSigsEtiologiesColors, 16
                                                                                                                                                      GetCOSMICMutSigsNames, 16
             PCAWG.Platinum.All.Technology.Related.Artଙ୍କୃଷ୍ଟେମ୍ପ୍ରେମ୍ପ୍ରେମ୍ବର
                                                                                                                                                      GetOptimizedSignatures, 18
             {\tt PCAWG.Possible.Sequencing.Artifact.Signat} \\ \textbf{Green} \\ \textbf{grameterLowerUpperVector}, \\ \textbf{18} \\ \textbf{20} \\ \textbf{
                                                                                                                                                      GetPCAWGMutSigs, 19
                                                                                                                                                      GetPCAWGMutSigsEtiologiesColors, 19
             PCAWG. Target. Mutational. Signatures,
                                                                                                                                                      GetPCAWGMutSigsNames, 20
                                                                                                                                                      GetPCAWGPlatinumMutSigs, 20
             TriNuc.Mutation.Type.Hex.Colors,
                                                                                                                                                      GetPCAWGPlatinumMutSigsEtiologiesColors,
AnnotateVCFObj, 4, 37, 46
                                                                                                                                                      GetPCAWGPlatinumMutSigsNames, 21
                                                                                                                                                      GetSeedForVCF, 21
CheckIfVariantRefinementIsNecessary, 5
Chromosome. Names, 6
                                                                                                                                                      InitializeVCF, 22
ComputeZScore, 6
                                                                                                                                                     Leaky.ReLU.A.Art.Obj.Fn, 22
ComputeZScoreEquiValue, 7
                                                                                                                                                     Leaky.ReLU.A.Ref.Obj.Fn, 23
DecimalCeiling, 7
                                                                                                                                                     Leaky.ReLU.Obj.Fn, 23
Default.Obj.Fn, 8
                                                                                                                                                     MakeFilter, 8, 24
DefaultFilterToBinary, 8
                                                                                                                                                     MutaliskParseVCFObj, 24
EnumerateTriNucCounts, 9
                                                                                                                                                     MutPatParseRefMutSigs, 25, 54
Euc.Exp.Weighted.Obj.Fn, 9
                                                                                                                                                     MutPatParseVCFObj, 25, 54
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.1,
                                                                                                                                                     ParameterToBits, 8, 26
                                                                                                                                                      ParseConfigFile, 26
Euc.Exp.Weighted.Seq.Art.Only.Obj.Fn.2,
                                                                                                                                                      PCAWG.All.Sequencing.Artifact.Signatures,
                          10
                                                                                                                                                                                27
Euc. Obj. Fn, 11
                                                                                                                                                      PCAWG.Known.Sequencing.Artifact.Signatures,
Exp. Weighted. A. Art. Obj. Fn, 11
Exp.Weighted.A.Ref.Obj.Fn, 12
                                                                                                                                                      PCAWG.Platinum.All.Technology.Related.Artifact.Signatures,
Exp.Weighted.Obj.Fn.1, 12
Exp.Weighted.Obj.Fn.2, 13
                                                                                                                                                      PCAWG.Possible.Sequencing.Artifact.Signatures,
Exp.Weighted.Refined.Seq.Art.Only.Obj.Fn,
                                                                                                                                                     PCAWG. Target. Mutational. Signatures, 28
FilterByStrandBiasAnalysis, 14
                                                                                                                                                     PerformStrandBiasAnalysis, 29
```

INDEX 61

```
PlotMutaliskResults, 29
                                                TriNuc.Mutation.Type.Hex.Colors, 57
PlotMutationTypes, 30
                                                UpdateFilter, 58
PlotOptimizationIterations, 31
PlotSignaturesContProbs, 32
                                                WriteFIREVATResultsToTSV, 58
PlotTable, 33
                                                WriteVCF, 59
PlotTriNucSpectrum, 34
PlotVCFStatsBoxPlots, 35
PlotVCFStatsHistograms, 36
PrepareAnnotationDB, 4, 37, 46, 50
PrepareArtifactAnnotationTable, 37
PrepareArtifactStrandBiasTable, 38
PrepareArtifactualMutsOptimizationIterationsPlot,
PrepareFilterCutoffsTable, 39
{\tt Prepare Genetic Algorithm Parameters Table},
{\tt PrepareIdentifiedSignaturesPlot}, 40
PrepareMLEReconstructedSpectrumsPlot,
PrepareNucleotideSubstitutionTypesPlot,
        41
PrepareObservedSpectrumsPlot, 41
PrepareOptimizationResultsTable, 42
PrepareOptimizedVCFStatisticsPlot, 42
PrepareRefinedAnnotationTable, 43
{\tt Prepare Refined Muts Optimization Iterations Plot},
        43
PrepareRefinedStrandBiasTable, 44
PrepareResidualSpectrumsPlot, 44
PrepareTrinucleotideSpectrumsTable, 45
PrintLog, 45
QueryAnnotatedVCF, 46
ReadOptimizationIterationReport, 46
ReadVCF, 4, 15, 26, 29, 37, 47
ReportFIREVATResults, 47
RunFIREVAT, 18, 37–47, 48
RunGAMode, 51
RunManualMode, 51
RunMutalisk, 30, 52
RunMutaliskHelper, 53
RunMutPat, 54
Sig.Extraction.Obj.Fn, 55
Sigmoid.Obj.Fn, 55
Test.Obj.Fn.1, 56
Test.Obj.Fn.2, 57
```