Package 'ICAMS'

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Title In-depth Characterization and Analysis of Mutational Signatures ('ICAMS')

Description Analysis and visualization of experimentally elucidated mutational

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Type Package

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```
signatures -- the kind of analysis and visualization in Boot et al.,
      ``In-depth characterization of the cisplatin mutational signature in
      human cell lines and in esophageal and liver tumors", Genome Research 2018,
      <doi:10.1101/gr.230219.117> and
      `Characterization of colibactin-associated mutational signature in an
      Asian oral squamous cell carcinoma and in other mucosal tumor types",
      Genome Research 2020 <doi:10.1101/gr.255620.119>.
      'ICAMS' stands for In-depth Characterization
      and Analysis of Mutational Signatures. 'ICAMS' has functions to read in
      variant call files (VCFs) and to collate the corresponding catalogs of
      mutational spectra and to analyze and plot catalogs of mutational spectra
      and signatures. Handles both ``counts-based" and ``density-based" catalogs
      of mutational spectra or signatures.
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2 R topics documented:

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${\sf R}$ topics documented:

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Description

An R list with one element each for BSgenome.Hsapiens.1000genomes.hs37d5, BSgenome.Hsapiens.UCSC.hg38 and BSgenome.Mmusculus.UCSC.mm10. Each element is in turn a sub-list keyed by exome, transcript, and genome. Each element of the sub list is keyed by the number of rows in the catalog class (as a string, e.g. "78", not 78). The keys are: 78 (DBS78Catalog), 96 (SBS96Catalog), 136 (DBS136Catalog), 144 (DBS144Catalog), 192 (SBS192Catalog), and 1536 (SBS1536Catalog). So, for example to get the exome abundances for SBS96 catalogs for BSgenome.Hsapiens.UCSC.hg38 exomes one would reference all.abundance[["BSgenome.Hsapiens.UCSC.hg38"]][["exome"]][["96"]] or all.abundance\$BSgenome.Hsapiens.UCSC.hg38\$exome\$"96". The value of the abundance is an integer vector with the K-mers as names and each value being the count of that K-mer.

Usage

all.abundance

Format

See Description.

Examples

```
all.abundance$BSgenome.Hsapiens.UCSC.hg38$transcript$`144`    # AA AC AG AT CA CC ...    # 90769160 57156295 85738416 87552737 83479655 63267896 ...    # There are 90769160 AAs on the sense strands of transcripts in    # this genome.
```

 ${\tt AnnotateDBSVCF}$

Add sequence context and transcript information to an in-memory DBS VCF

Description

Add sequence context and transcript information to an in-memory DBS VCF

```
AnnotateDBSVCF(DBS.vcf, ref.genome, trans.ranges = NULL)
```

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Arguments

```
DBS.vcf An in-memory DBS VCF as a data.frame.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome.Hsapiens.1000genomes.hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10
```

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

Value

An in-memory DBS VCF as a data.table. This has been annotated with the sequence context (column name seq.21bases) and with transcript information in the form of a gene symbol (e.g. "TP53") and transcript strand. This information is in the columns trans.start.pos, trans.end.pos, trans.strand, trans.Ensembl.gene.ID and trans.gene.symbol in the output. These columns are not added if is.null(trans.ranges).

Examples

AnnotateIDVCF

Add sequence context to an in-memory ID (insertion/deletion) VCF, and confirm that they match the given reference genome

Description

Add sequence context to an in-memory ID (insertion/deletion) VCF, and confirm that they match the given reference genome

```
AnnotateIDVCF(
   ID.vcf,
   ref.genome,
   flag.mismatches = 0,
   name.of.VCF = NULL,
   suppress.discarded.variants.warnings = TRUE
)
```

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Arguments

ID.vcf An in-memory ID (insertion/deletion) VCF as a data.frame. This function

expects that there is a "context base" to the left, for example REF = ACG, ALT

= A (deletion of CG) or REF = A, ALT = ACC (insertion of CC).

ref.genome A ref.genome argument as described in ICAMS.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants. See element discarded.variants in the return value for more details.

name.of.VCF Name of the VCF file. suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A list of elements:

- annotated.vcf: The original VCF data frame with two new columns added to the input data frame:
 - seq. context: The sequence embedding the variant.
 - seq.context.width: The width of seq.context to the left.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

Examples

AnnotateSBSVCF

Add sequence context and transcript information to an in-memory SBS VCF

Description

Add sequence context and transcript information to an in-memory SBS VCF

```
AnnotateSBSVCF(SBS.vcf, ref.genome, trans.ranges = NULL)
```

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Arguments

```
SBS.vcf An in-memory SBS VCF as a data.frame.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome.Hsapiens.1000genomes.hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10
```

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

Value

An in-memory SBS VCF as a data.table. This has been annotated with the sequence context (column name seq.21bases) and with transcript information in the form of a gene symbol (e.g. "TP53") and transcript strand. This information is in the columns trans.start.pos, trans.end.pos, trans.strand, trans.Ensembl.gene.ID and trans.gene.symbol in the output. These columns are not added if is.null(trans.ranges).

Examples

as.catalog

Create a catalog from a matrix, data.frame, or vector

Description

Create a catalog from a matrix, data.frame, or vector

```
as.catalog(
  object,
  ref.genome = NULL,
  region = "unknown",
  catalog.type = "counts",
  abundance = NULL,
  infer.rownames = FALSE
)
```

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Arguments

object A numeric matrix, numeric data.frame, or vector. If a vector, converted

to a 1-column matrix with rownames taken from the element names of the vector and with column name "Unknown". If argument infer.rownames is FALSE than this argument must have rownames to denote the mutation types.

See CatalogRowOrder for more details.

ref.genome A ref.genome argument as described in ICAMS.

region A character string designating a region, one of genome, transcript, exome,

unknown; see ICAMS.

catalog.type One of "counts", "density", "counts.signature", "density.signature".

abundance If NULL, then inferred if ref.genome is one of the reference genomes known

to ICAMS and region is not unknown. See ICAMS. The argument abundance should contain the counts of different source sequences for mutations in the

same format as the numeric vectors in all. abundance.

infer.rownames If TRUE, and object has no rownames, then assume the rows of object are

in the correct order and add the rownames implied by the number of rows in object (e.g. rownames for SBS 192 if there are 192 rows). If TRUE, **be sure the**

order of rows is correct.

Value

A catalog as described in ICAMS.

Examples

Canonicalize1Del

Given a deletion and its sequence context, categorize it

Description

This function is primarily for internal use, but we export it to document the underlying logic.

Usage

```
Canonicalize1Del(context, del.seq, pos, trace = 0)
```

Arguments

context The deleted sequence plus ample surrounding sequence on each side (at least as

long as del.seq).

del.seq The deleted sequence in context.

pos The position of del. sequence in context.

trace If > 0, then generate messages tracing how the computation is carried out.

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Details

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2017_12_08.xlsx for additional information on deletion mutation classification.

This function first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Value

A string that is the canonical representation of the given deletion type. Return NA and raise a warning if there is an un-normalized representation of the deletion of a repeat unit. See FindDelMH for details. (This seems to be very rare.)

Examples

```
Canonicalize1Del("xyAAAqr", del.seq = "A", pos = 3) # "DEL:T:1:2"
Canonicalize1Del("xyAAAqr", del.seq = "A", pos = 4) # "DEL:T:1:2"
Canonicalize1Del("xyAqr", del.seq = "A", pos = 3) # "DEL:T:1:0"
```

CatalogRowOrder

Standard order of row names in a catalog

Description

This data is designed for those who need to create their own catalogs from formats not supported by this package. The rownames denote the mutation types. For example, for SBS96 catalogs, the rowname AGAT represents a mutation from AGA > ATA.

Usage

```
catalog.row.order
catalog.row.order.sp
```

Format

A list of character vectors indicating the standard orders of row names in catalogs.

An object of class list of length 8.

An object of class list of length 4.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

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See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+. In ID83 catalogs, deletion repeat sizes range from 0 to 5.

Examples

```
catalog.row.order$SBS96
# "ACAA" "ACCA" "ACGA" "ACTA" "CCAA" "CCCA" "CCGA" "CCTA" ...
# There are altogether 96 row names to denote the mutation types
# in SBS96 catalog.

catalog.row.order.sp$ID83
# "DEL:C:1:0" "DEL:C:1:1" "DEL:C:1:2" "DEL:C:1:3" ...
# There are altogether 83 row names to denote the mutation types
# in ID83 catalog.
```

CollapseCatalog

"Collapse" a catalog

Description

- 1. Take a mutational spectrum or signature catalog that is based on a fined-grained set of features (for example, single-nucleotide substitutions in the context of the preceding and following 2 bases).
- 2. Collapse it to a catalog based on a coarser-grained set of features (for example, single-nucleotide substitutions in the context of the immediately preceding and following bases).

Collapse192CatalogTo96 Collapse an SBS 192 catalog to an SBS 96 catalog.

Collapse1536CatalogTo96 Collapse an SBS 1536 catalog to an SBS 96 catalog.

Collapse144CatalogTo78 Collapse a DBS 144 catalog to a DBS 78 catalog.

Usage

```
Collapse192CatalogTo96(catalog)
Collapse1536CatalogTo96(catalog)
Collapse144CatalogTo78(catalog)
```

Arguments

catalog

A catalog as defined in ICAMS.

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Value

A catalog as defined in ICAMS.

Examples

FindDelMH

Return the length of microhomology at a deletion

Description

Return the length of microhomology at a deletion

Usage

```
FindDelMH(context, deleted.seq, pos, trace = 0, warn.cryptic = TRUE)
```

Arguments

context The deleted sequence plus ample surrounding sequence on each side (at least as

long as del. sequence).

deleted.seq The deleted sequence in context.

pos The position of del. sequence in context.

trace If > 0, then generate various messages showing how the computation is carried

out.

warn.cryptic if TRUE generating a warning if there is a cryptic repeat (see the example).

Details

This function is primarily for internal use, but we export it to document the underlying logic.

Example:

GGCTAGTT aligned to GGCTAGAACTAGTT with a deletion represented as:

```
GGCTAGAACTAGTT
GG-----CTAGTT GGCTAGTT GG[CTAGAA]CTAGTT
----
```

Presumed repair mechanism leading to this:

```
GGCTAGAACTAGTT
```

=>

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```
GGCTAG TT
CC GATCAA
....

=>

GGCTAGTT
CCGATCAA
```

Variant-caller software can represent the same deletion in several different, but completely equivalent, ways.

```
GGCTAGTT GGCTAGTT GGC[TAGAAC]TAGTT

* --- * ---

GGCT-----AGTT GGCTAGTT GGCT[AGAACT]AGTT

** -- ** --

GGCTA-----GTT GGCTAGTT GGCTA[GAACTA]GTT

*** - *** -

GGCTAG----TT GGCTAGTT GGCTAG[AACTAG]TT

**** ****
```

This function finds:

- 1. The maximum match of undeleted sequence to the left of the deletion that is identical to the right end of the deleted sequence, and
- 2. The maximum match of undeleted sequence to the right of the deletion that is identical to the left end of the deleted sequence.

The microhomology sequence is the concatenation of items (1) and (2).

Warning

A deletion in a *repeat* can also be represented in several different ways. A deletion in a repeat is abstractly equivalent to a deletion with microhomology that spans the entire deleted sequence. For example;

```
GACTAGCTAGTT
GACTAGTT GACTAGTT GACTA[GCTA]GTT

*** -*** -

is really a repeat

GACTAG----TT GACTAGTT GACTAG[CTAG]TT

**** ----

GACT----AGTT GACTAGTT GACT[AGCT]AGTT

** --* --
```

This function only flags these "cryptic repeats" with a -1 return; it does not figure out the repeat extent.

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Value

The length of the maximum microhomology of del. sequence in context.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Examples

FindMaxRepeatDel

Return the number of repeat units in which a deletion is embedded

Description

Return the number of repeat units in which a deletion is embedded

```
FindMaxRepeatDel(context, rep.unit.seq, pos)
```

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Arguments

context A string that embeds rep.unit.seq at position pos

rep.unit.seq A substring of context at pos to pos + nchar(rep.unit.seq) -1, which is the

repeat unit sequence.

pos The position of rep.unit.seq in context.

Details

This function is primarily for internal use, but we export it to document the underlying logic.

For example FindMaxRepeatDel("xyaczt", "ac", 3) returns 0.

If substr(context, pos, pos + nchar(rep.unit.seq) -1) != rep.unit.seq then stop.

If this functions returns 0, then it is necessary to look for microhomology using the function FindDelMH.

Warning

This function depends on the variant caller having "aligned" the deletion within the context of the repeat.

For example, a deletion of CAG in the repeat

GTCAGCAGCATGT

can have 3 "aligned" representations as follows:

CT---CAGCAGGT CTCAG---CAGGT CTCAGCAG---GT

In these cases this function will return 2. (Please not that the return value does not include the rep.uni.seq in the count.)

However, the same deletion can also have an "unaligned" representation, such as

CTCAGC---AGGT

(a deletion of AGC).

In this case this function will return 1 (a deletion of AGC in a 2-element repeat of AGC).

Value

The number of repeat units in which rep.unit.seq is embedded, not including the input rep.unit.seq in the count.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

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Examples

```
FindMaxRepeatDel("xyACACzt", "AC", 3) # 1
FindMaxRepeatDel("xyACACzt", "CA", 4) # 0
```

GeneExpressionData

Example gene expression data from two cell lines

Description

This data is designed to be used as an example in function PlotTransBiasGeneExpToPdf.

Usage

```
gene.expression.data.HepG2
gene.expression.data.MCF10A
```

Format

A data.table which contains the expression values of genes.

An object of class data.table (inherits from data.frame) with 57736 rows and 4 columns.

An object of class data.table (inherits from data.frame) with 57736 rows and 4 columns.

Examples

```
gene.expression.data.HepG2
# Ensembl.gene.ID gene.symbol counts
                                           TPM
# ENSG00000000003 TSPAN6 6007 33.922648455
# ENSG00000000005
                    TNMD
                             0 0.000000000
                     DPM1
# ENSG00000000419
                            4441 61.669371091
                    SCYL3 1368 3.334619195
# ENSG00000000457
                           916
# ENSG00000000460
                C1orf112
                                   2.416263423
```

GetVAF

Extract the VAFs (variant allele frequencies) and read depth information from a VCF file

Description

Extract the VAFs (variant allele frequencies) and read depth information from a VCF file

```
GetStrelkaVAF(vcf, name.of.VCF = NULL)
GetMutectVAF(vcf, name.of.VCF = NULL, tumor.col.name = NA)
GetFreebayesVAF(vcf, name.of.VCF = NULL)
```

Arguments

vcf Said VCF as a data.frame.

name.of.VCF Name of the VCF file.

 $tumor.col.name \quad Optional. \ Only \ applicable \ to \ \textbf{Mutect} \ VCF. \ Name \ of \ the \ column \ in \ \textbf{Mutect} \ VCF.$

which contains the tumor sample information. It \pmb{must} have quotation marks. If tumor.col.name is equal to NA(default), this function will use the 10th column

to calculate VAFs.

Value

The original vcf with two additional columns added which contain the VAF(variant allele frequency) and read depth information.

Examples

ICAMS

ICAMS: In-depth Characterization and Analysis of Mutational Signatures

Description

Analysis and visualization of experimentally elucidated mutational signatures – the kind of analysis and visualization in Boot et al., "In-depth characterization of the cisplatin mutational signature in human cell lines and in esophageal and liver tumors",

Genome Research 2018 https://doi.org/10.1101/gr.230219.117 and "Characterization of colibactin-associated mutational signature in an Asian oral squamous cell carcinoma and in other mucosal tumor types", Genome Research 2020, https://doi.org/10.1101/gr.255620.119. "ICAMS" stands for In-depth Characterization and Analysis of Mutational Signatures. "ICAMS" has functions to read in variant call files (VCFs) and to collate the corresponding catalogs of mutational spectra and to analyze and plot catalogs of mutational spectra and signatures. Handles both "counts-based" and "density-based" catalogs of mutational spectra or signatures.

Details

"ICAMS" can read in VCFs generated by Strelka or Mutect, and collate the mutations into "catalogs" of mutational spectra. "ICAMS" can create and plot catalogs of mutational spectra or signatures for single base substitutions (SBS), double base substitutions (DBS), and small insertions and deletions (ID). It can also read and write these catalogs.

Catalogs

A key data type in "ICAMS" is a "catalog" of mutation counts, of mutation densities, or of mutational signatures.

Catalogs are S3 objects of class matrix and one of several additional classes that specify the types of the mutations represented in the catalog. The possible additional class is one of

- SBS96Catalog (strand-agnostic single base substitutions in trinucleotide context)
- SBS192Catalog (transcription-stranded single-base substitutions in trinucleotide context)
- SBS1536Catalog
- DBS78Catalog
- DBS144Catalog
- DBS136Catalog
- IndelCatalog

as.catalog is the main constructor.

Conceptually, a catalog also has one of the following types, indicated by the attribute catalog. type:

- 1. Matrix of mutation counts (one column per sample), representing (counts-based) mutational spectra (catalog.type = "counts").
- 2. Matrix of mutation densities, i.e. mutations per occurrences of source sequences (one column per sample), representing (density-based) mutational spectra (catalog.type = "density").
- 3. Matrix of mutational signatures, which are similar to spectra. However where spectra consist of counts or densities of mutations in each mutation class (e.g. ACA > AAA, ACA > AGA, ACA > ATA, ACC > AAC, ...), signatures consist of the proportions of mutations in each class (with all the proportions summing to 1). A mutational signature can be based on either:
 - mutation counts (a "counts-based mutational signature", catalog.type = "counts.signature"), or
 - mutation densities (a "density-based mutational signature", catalog.type = "density.signature").

Catalogs also have the attribute abundance, which contains the counts of different source sequences for mutations. For example, for SBSs in trinucleotide context, the abundances would be the counts of each trinucleotide in the human genome, exome, or in the transcribed region of the genome. See TransformCatalog for more information. Abundances logically depend on the species in question and on the part of the genome being analyzed.

In "ICAMS" abundances can sometimes be inferred from the catalog class attribute and the function arguments region, ref.genome, and catalog.type. Otherwise abundances can be provided as an abundance argument. See all.abundance for examples.

Possible values for region are the strings genome, transcript, exome, and unknown; transcript includes entire transcribed regions, i.e. the introns as well as the exons.

If you need to create a catalog from a source other than this package (i.e. other than with ReadCatalog or StrelkaSBSVCFFilesToCatalog, MutectVCFFilesToCatalog, etc.), then use as.catalog.

Creating catalogs from variant call files (VCF files)

1. VCFsToCatalogs creates 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and ID (small insertion and deletion) catalog from the VCFs. It has more general usage with functionalities overlapping with the three functions below. For example, it is the same as MutectVCFFilesToCatalog when variant.caller = "mutect".

2. StrelkaSBSVCFFilesToCatalog creates 3 SBS catalogs (96, 192, 1536) and 3 DBS catalogs (78, 136, 144) from the Strelka SBS VCFs.

- 3. StrelkaIDVCFFilesToCatalog creates an ID (small insertion and deletion) catalog from the Strelka ID VCFs.
- 4. MutectVCFFilesToCatalog creates 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and ID (small insertion and deletion) catalog from the Mutect VCFs.

Plotting catalogs

The PlotCatalog functions plot mutational spectra for **one** sample or plot **one** mutational signature. The PlotCatalogToPdf functions plot catalogs of mutational spectra or of mutational signatures to a PDF file.

Wrapper functions to create catalogs from VCFs and plot the catalogs to PDF files

- 1. VCFsToCatalogsAndPlotToPdf creates all types of SBS, DBS and ID catalogs from VCFs and plots the catalogs. It has more general usage with functionalities overlapping with the three functions below. For example, it is the same as MutectVCFFilesToCatalogAndPlotToPdf when variant.caller = "mutect".
- 2. StrelkaSBSVCFFilesToCatalogAndPlotToPdf creates all type of SBS and DBS catalogs from Strelka SBS VCFs and plots the catalogs.
- 3. StrelkaIDVCFFilesToCatalogAndPlotToPdf creates an ID (small insertion and deletion) catalog from Strelka ID VCFs and plot it.
- 4. MutectVCFFilesToCatalogAndPlotToPdf creates all types of SBS, DBS and ID catalogs from Mutect VCFs and plots the catalogs.

Wrapper functions to create a zip file which contains catalogs and plot PDFs from VCF files

- VCFsToZipFile creates a zip file which contains SBS, DBS and ID catalogs and plot PDFs from VCF files. It has more general usage with functionalities overlapping with the three functions below. For example, it is the same as MutectVCFFilesToZipFile when variant.caller = "mutect".
- 2. StrelkaSBSVCFFilesToZipFile creates a zip file which contains SBS and DBS catalogs and plot PDFs from Strelka SBS VCF files.
- 3. StrelkaIDVCFFilesToZipFile creates a zip file which contains ID (small insertion and deletion) catalog and plot PDF from Strelka ID VCF files.
- 4. MutectVCFFilesToZipFile creates a zip file which contains SBS, DBS and ID catalogs and plot PDFs from Mutect VCF files.

The ref.genome (reference genome) argument

Many functions take the argument ref.genome.

To create a mutational spectrum catalog from a VCF file, ICAMS needs the reference genome sequence that matches the VCF file. The ref. genome argument provides this.

ref.genome must be one of

- 1. A variable from the Bioconductor BSgenome package that contains a particular reference genome, for example BSgenome. Hsapiens. 1000genomes. hs37d5.
- 2. The strings "hg38" or "GRCh38", which specify BSgenome. Hsapiens. UCSC. hg38.
- 3. The strings "hg19" or "GRCh37", which specify BSgenome. Hsapiens. 1000genomes. hs37d5.

4. The strings "mm10" or "GRCm38", which specify BSgenome. Mmusculus. UCSC. mm10.

All needed reference genomes must be installed separately by the user. Further instructions are at https://bioconductor.org/packages/release/bioc/html/BSgenome.html.

Use of ICAMS with reference genomes other than the 2 human genomes and 1 mouse genome specified above is restricted to catalog.type of counts or counts.signature unless the user also creates the necessary abundance vectors. See all.abundance.

Use available.genomes() to get the list of available genomes.

Writing catalogs to files

The WriteCatalog functions write a catalog to a file.

Reading catalogs

The ReadCatalog functions read a file that contains a catalog in standardized format.

Transforming catalogs

The TransformCatalog function transforms catalogs of mutational spectra or signatures to account for differing abundances of the source sequence of the mutations in the genome.

For example, mutations from ACG are much rarer in the human genome than mutations from ACC simply because CG dinucleotides are rare in the genome. Consequently, there are two possible representations of mutational spectra or signatures. One representation is based on mutation counts as observed in a given genome or exome, and this approach is widely used, as, for example, at https://cancer.sanger.ac.uk/cosmic/signatures, which presents signatures based on observed mutation counts in the human genome. We call these "counts-based spectra" or "counts-based signatures".

Alternatively, mutational spectra or signatures can be represented as mutations per source sequence, for example the number of ACT > AGT mutations occurring at all ACT 3-mers in a genome. We call these "density-based spectra" or "density-based signatures".

This function can also transform spectra based on observed genome-wide counts to "density"-based catalogs. In density-based catalogs mutations are expressed as mutations per source sequences. For example, a density-based catalog represents the proportion of ACCs mutated to ATCs, the proportion of ACGs mutated to ATGs, etc. This is different from counts-based mutational spectra catalogs, which contain the number of ACC > ATC mutations, the number of ACG > ATG mutations, etc.

This function can also transform observed-count based spectra or signatures from genome to exome based counts, or between different species (since the abundances of source sequences vary between genome and exome and between species).

Collapsing catalogs

The CollapseCatalog functions

- 1. Take a mutational spectrum or signature catalog that is based on a fined-grained set of features (for example, single-nucleotide substitutions in the context of the preceding and following 2 bases).
- 2. Collapse it to a catalog based on a coarser-grained set of features (for example, single-nucleotide substitutions in the context of the immediately preceding and following bases).

Data

- 1. CatalogRowOrder Standard order of rownames in a catalog. The rownames encode the type of each mutation. For example, for SBS96 catalogs, the rowname AGAT represents a mutation from AGA > ATA.
- 2. TranscriptRanges Transcript ranges and strand information for a particular reference genome.
- 3. GeneExpressionData Example gene expression data from two cell lines.

MutectVCFFilesToCatalog

Create SBS, DBS and Indel catalogs from Mutect VCF files

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the Mutect VCFs specified by files

Usage

```
MutectVCFFilesToCatalog(
   files,
   ref.genome,
   trans.ranges = NULL,
   region = "unknown",
   names.of.VCFs = NULL,
   tumor.col.names = NA,
   flag.mismatches = 0,
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Mutect VCF files.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

- 1. BSgenome. Hsapiens. 1000genomes. hs37d5
- 2. BSgenome.Hsapiens.UCSC.hg38
- 3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Character vector of column names in VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the VCFs to calculate VAFs. See GetMutectVAF for more details.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls VCFsToSBSCatalogs, VCFsToDBSCatalogs and VCFsToIDCatalogs

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID.class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <- custom. abundance.

Examples

 ${\tt MutectVCFFilesToCatalogAndPlotToPdf}$

Create SBS, DBS and Indel catalogs from Mutect VCF files and plot them to PDF

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the Mutect VCFs specified by files and plot them to PDF

```
MutectVCFFilesToCatalogAndPlotToPdf(
   files,
   ref.genome,
   trans.ranges = NULL,
   region = "unknown",
   names.of.VCFs = NULL,
   tumor.col.names = NA,
   output.file = "",
   flag.mismatches = 0,
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Mutect VCF files.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome. Hsapiens. 1000 genomes. hs37d5

2. BSgenome. Hsapiens. UCSC. hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region A character string designating a genomic region; see as . catalog and ICAMS.

names.of.VCFs Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Character vector of column names in VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the VCFs to calculate VAFs. See GetMutectVAF for more details.

output.file Optional. The base name of the PDF files to be produced; multiple files will be generated, each ending in x.pdf, where x indicates the type of catalog plotted in the file.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls MutectVCFFilesToCatalog and PlotCatalogToPdf

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).

- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class,
 DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID.class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

MutectVCFFilesToZipFile

Create a zip file which contains catalogs and plot PDFs from Mutect VCF files

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the Mutect VCFs specified by dir, save the catalogs as CSV files, plot them to PDF and generate a zip archive of all the output files.

Usage

```
MutectVCFFilesToZipFile(
  dir,
  zipfile,
  ref.genome,
  trans.ranges = NULL,
  region = "unknown",
  names.of.VCFs = NULL
  tumor.col.names = NA,
  base.filename = "",
  flag.mismatches = 0,
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

dir

Pathname of the directory which contains only the Mutect VCF files. Each Mutect VCF must have a file extension ".vcf" (case insensitive) and share the

same ref.genome and region.

zipfile

Pathname of the zip file to be created.

ref.genome

A ref. genome argument as described in ICAMS.

trans.ranges

Optional. If ref. genome specifies one of the BSgenome object

- 1. BSgenome. Hsapiens. 1000 genomes. hs37d5
- 2. BSgenome.Hsapiens.UCSC.hg38
- 3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as. catalog and ICAMS.

names.of.VCFs

Optional. Character vector of names of the VCF files. The order of names in names. of . VCFs should match the order of VCFs listed in dir. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in dir and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Character vector of column names in VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of VCFs listed in dir. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the VCFs to calculate VAFs. See GetMutectVAF for more details.

base.filename

Optional. The base name of the CSV and PDF files to be produced; multiple files will be generated, each ending in x. csv or x. pdf, where x indicates the type of catalog.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls MutectVCFFilesToCatalog, PlotCatalogToPdf, WriteCatalog and zipr.

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144)
- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID.class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

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See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

PlotCatalog

Plot one spectrum or signature

Description

Plot the spectrum of **one** sample or plot **one** signature. The type of graph is based on one attribute("catalog.type") of the input catalog. You can first use TransformCatalog to get different types of catalog and then do the plotting.

```
PlotCatalog(
  catalog,
  plot.SBS12 = NULL,
  cex = NULL,
  grid = NULL,
  upper = NULL,
  xlabels = NULL,
  ylim = NULL)
```

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Arguments

catalog	A catalog as defined in ICAMS with attributes added. See as.catalog for more details.
plot.SBS12	Only meaningful for class SBS192Catalog; if TRUE, generate an abbreviated plot of only SBS without context, i.e. C>A, C>G, C>T, T>A, T>C, T>G each on transcribed and untranscribed strands, rather than SBS in trinucleotide context, e.g. $ACA > AAA$, $ACA > AGA$,, $TCT > TAT$,
cex	Has the usual meaning. Taken from par ("cex") by default. Only implemented for SBS96Catalog, SBS192Catalog and DBS144Catalog.
grid	A logical value indicating whether to draw grid lines. Only implemented for SBS96Catalog.
upper	A logical value indicating whether to draw horizontal lines and the names of major mutation class on top of graph. Only implemented for SBS96Catalog.
xlabels	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog. If FALSE then plot x axis tick marks; set $par(tck = 0)$ to suppress.
ylim	Has the usual meaning. Only implemented for SBS96Catalog and IndelCatalog.

Value

An **invisible** list whose first element is a logic value indicating whether the plot is successful. For SBS96Catalog, SBS192Catalog, DBS78Catalog, DBS144Catalog and IndelCatalog, the list will have a second element, which is a numeric vector giving the coordinates of all the bar midpoints drawn, useful for adding to the graph. For **SBS192Catalog** with "counts" catalog.type and non-NULL abundance and plot.SBS12 = TRUE, the list will have an additional element which is a list containing the strand bias statistics.

Comments

For **SBS192Catalog** with "counts" catalog.type and non-NULL abundance and plot . SBS12 = TRUE, the strand bias statistics are Benjamini-Hochberg q-values based on two-sided binomial tests of the mutation counts on the transcribed and untranscribed strands relative to the actual abundances of C and T on the transcribed strand. On the SBS12 plot, asterisks indicate q-values as follows *, Q < 0.05; **, Q < 0.01; ***, Q < 0.001.

Note

The sizes of repeats involved in deletions range from 0 to 5+ in the mutational-spectra and signature catalog rownames, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

28 PlotCatalogToPdf

PlotCatalogToPdf Plot catalog to a PDF file

Description

Plot catalog to a PDF file. The type of graph is based on one attribute("catalog.type") of the input catalog. You can first use TransformCatalog to get different types of catalog and then do the plotting.

Usage

```
PlotCatalogToPdf(
  catalog,
  file,
  plot.SBS12 = NULL,
  cex = NULL,
  grid = NULL,
  upper = NULL,
  xlabels = NULL,
  ylim = NULL
)
```

Arguments

catalog	A catalog as defined in ICAMS with attributes added. See as.catalog for more details.
file	The name of the PDF file to be produced.
plot.SBS12	Only meaningful for class SBS192Catalog; if TRUE, generate an abbreviated plot of only SBS without context, i.e. C>A, C>G, C>T, T>A, T>C, T>G each on transcribed and untranscribed strands, rather than SBS in trinucleotide context, e.g. ACA > AAA, ACA > AGA,, TCT > TAT, There are 12 bars in the graph.
cex	Has the usual meaning. A default value has been used by the program internally. Only implemented for SBS96Catalog, SBS192Catalog and DBS144Catalog.
grid	A logical value indicating whether to draw grid lines. Only implemented for SBS96Catalog.
upper	A logical value indicating whether to draw horizontal lines and the names of major mutation class on top of graph. Only implemented for SBS96Catalog.
xlabels	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog. If FALSE then plot x axis tick marks; set $par(tck = 0)$ to suppress.
ylim	Has the usual meaning. Only implemented for SBS96Catalog and IndelCatalog.

Value

An **invisible** list whose first element is a logic value indicating whether the plot is successful. For **SBS192Catalog** with "counts" catalog.type and non-null abundance and plot.SBS12 = TRUE, the list will have a second element which is a list containing the strand bias statistics.

Comments

For **SBS192Catalog** with "counts" catalog.type and non-NULL abundance and plot . SBS12 = TRUE, the strand bias statistics are Benjamini-Hochberg q-values based on two-sided binomial tests of the mutation counts on the transcribed and untranscribed strands relative to the actual abundances of C and T on the transcribed strand. On the SBS12 plot, asterisks indicate q-values as follows *, Q < 0.05; **, Q < 0.01; ***, Q < 0.001.

Note

The sizes of repeats involved in deletions range from 0 to 5+ in the mutational-spectra and signature catalog rownames, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

PlotTransBiasGeneExp

Plot transcription strand bias with respect to gene expression values

Description

Plot transcription strand bias with respect to gene expression values

Usage

```
PlotTransBiasGeneExp(
  annotated.SBS.vcf,
  expression.data,
  Ensembl.gene.ID.col,
  expression.value.col,
  num.of.bins,
  plot.type,
  damaged.base = NULL,
  ymax = NULL
)
```

Arguments

```
annotated.SBS.vcf
```

An SBS VCF annotated by AnnotateSBSVCF. It **must** have transcript range information added.

expression.data

A data.table which contains the expression values of genes.

See GeneExpressionData for more details.

Ensembl.gene.ID.col

Name of column which has the Ensembl gene ID information in expression.data.

expression.value.col

Name of column which has the gene expression values in expression.data.

num.of.bins The number of bins that will be plotted on the graph.

plot.type A character string indicating one mutation type to be plotted. It should be one

of "C>A", "C>G", "C>T", "T>A", "T>C", "T>G".

damaged.base One of NULL, "purine" or "pyrimidine". This function allocates approxi-

mately equal numbers of mutations from damaged.base into each of num.of.bins bin by expression level. E.g. if damaged.base is "purine", then mutations from A and G will be allocated in approximately equal numbers to each expression-level bin. The rationale for the name damaged.base is that the direction of strand bias is a result of whether the damage occurs on a purine or pyrimidine. If NULL, the function attempts to infer the damaged.base based on mutation

counts.

ymax Limit for the y axis. If not specified, it defaults to NULL and the y axis limit

equals 1.5 times of the maximum mutation counts in a specific mutation type.

Value

A list whose first element is a logic value indicating whether the plot is successful. The second element is a named numeric vector containing the p-values printed on the plot.

Note

The p-values are calculated by logistic regression using function glm. The dependent variable is labeled "1" and "0" if the mutation from annotated SBS vcf falls onto the untranscribed and transcribed strand respectively. The independent variable is the binary logarithm of the gene expression value from expression data plus one, i.e. $log_2(x+1)$ where x stands for gene expression value.

Examples

PlotTransBiasGeneExpToPdf

Plot transcription strand bias with respect to gene expression values to a PDF file

Description

Plot transcription strand bias with respect to gene expression values to a PDF file

Usage

```
PlotTransBiasGeneExpToPdf(
  annotated.SBS.vcf,
  file.
  expression.data,
  Ensembl.gene.ID.col,
  expression.value.col,
  num.of.bins,
  plot.type = c("C>A", "C>G", "C>T", "T>A", "T>C", "T>G"),
  damaged.base = NULL
)
```

Arguments

annotated.SBS.vcf

An SBS VCF annotated by AnnotateSBSVCF. It must have transcript range information added.

file The name of output file.

expression.data

A data. table which contains the expression values of genes.

See GeneExpressionData for more details.

Ensembl.gene.ID.col

Name of column which has the Ensembl gene ID information in expression. data.

expression.value.col

Name of column which has the gene expression values in expression.data.

num.of.bins

The number of bins that will be plotted on the graph.

plot.type

A vector of character indicating types to be plotted. It can be one or more types from "C>A", "C>G", "C>T", "T>A", "T>C", "T>G". The default is to print all

the six mutation types.

damaged.base

One of NULL, "purine" or "pyrimidine". This function allocates approximately equal numbers of mutations from damaged.base into each of num. of. bins bin by expression level. E.g. if damaged.base is "purine", then mutations from A and G will be allocated in approximately equal numbers to each expressionlevel bin. The rationale for the name damaged base is that the direction of strand bias is a result of whether the damage occurs on a purine or pyrimidine. If NULL, the function attempts to infer the damaged base based on mutation

counts.

Value

A list whose first element is a logic value indicating whether the plot is successful. The second element is a named numeric vector containing the p-values printed on the plot.

Note

The p-values are calculated by logistic regression using function glm. The dependent variable is labeled "1" and "0" if the mutation from annotated . SBS . vcf falls onto the untranscribed and transcribed strand respectively. The independent variable is the binary logarithm of the gene expression value from expression data plus one, i.e. $log_2(x+1)$ where x stands for gene expression value.

Examples

```
file <- c(system.file("extdata/Strelka-SBS-vcf/",</pre>
                       "Strelka.SBS.GRCh37.s1.vcf",
                       package = "ICAMS"))
list.of.vcfs <- ReadAndSplitStrelkaSBSVCFs(file)</pre>
SBS.vcf <- list.of.vcfs$SBS.vcfs[[1]]</pre>
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  annotated.SBS.vcf <- AnnotateSBSVCF(SBS.vcf, ref.genome = "hg19",</pre>
                                        trans.ranges = trans.ranges.GRCh37)
  PlotTransBiasGeneExpToPdf(annotated.SBS.vcf = annotated.SBS.vcf,
                             expression.data = gene.expression.data.HepG2,
                             Ensembl.gene.ID.col = "Ensembl.gene.ID",
                             expression.value.col = "TPM",
                             num.of.bins = 4,
                             plot.type = c("C>A","C>G","C>T","T>A","T>C"),
                             file = file.path(tempdir(), "test.pdf"))
}
```

ReadAndSplitMutectVCFs

Read and split Mutect VCF files

Description

Read and split Mutect VCF files

Usage

```
ReadAndSplitMutectVCFs(
   files,
   names.of.VCFs = NULL,
   tumor.col.names = NA,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files

Character vector of file paths to the Mutect VCF files.

 ${\tt names.of.VCFs}$

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Character vector of column names in VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the VCFs to calculate VAFs. See GetMutectVAF for more details.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A list containing the following objects:

- SBS: List of VCFs with only single base substitutions.
- DBS: List of VCFs with only doublet base substitutions as called by Mutect.
- ID: List of VCFs with only small insertions and deletions.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

See Also

```
MutectVCFFilesToCatalog
```

Examples

ReadAndSplitStrelkaSBSVCFs

Read and split Strelka SBS VCF files

Description

The function will find and merge adjacent SBS pairs into DBS if their VAFs are very similar. The default threshold value for VAF is 0.02.

Usage

```
ReadAndSplitStrelkaSBSVCFs(
  files,
  names.of.VCFs = NULL,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files

Character vector of file paths to the Strelka SBS VCF files.

names.of.VCFs

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

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Value

A list of elements as follows:

- SBS.vcfs: List of data.frames of pure SBS mutations no DBS or 3+BS mutations.
- DBS.vcfs: List of data.frames of pure DBS mutations no SBS or 3+BS mutations.
- · discarded.variants: Non-NULL only if there are variants that were excluded from the analysis. See the added extra column discarded reason for more details.

See Also

StrelkaSBSVCFFilesToCatalog

Examples

```
file <- c(system.file("extdata/Strelka-SBS-vcf",</pre>
                        "Strelka.SBS.GRCh37.s1.vcf",
                        package = "ICAMS"))
list.of.vcfs <- ReadAndSplitStrelkaSBSVCFs(file)</pre>
```

ReadAndSplitVCFs

Read and split VCF files

Description

Read and split VCF files

Usage

```
ReadAndSplitVCFs(
  files.
  variant.caller = "unknown",
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = NULL,
  get.vaf.function = NULL,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files

Character vector of file paths to the VCF files.

variant.caller Name of the variant caller that produces the VCF, can be either strelka, mutect or freebayes. This information is needed to calculate the VAFs (variant allele frequencies). If "unknown" (default) and get.vaf.function is NULL, then VAF and read depth will be NAs.

names.of.VCFs

Character vector of names of the VCF files. The order of names in names . of . VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

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tumor.col.names

Optional. Only applicable to **Mutect** VCFs. Character vector of column names in **Mutect** VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of **Mutect** VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the **Mutect** VCFs to calculate VAFs. See GetMutectVAF for more details.

filter.status

The status indicating a variant has passed all filters. An example would be "PASS". Variants which don't have the specified filter.status in the FILTER column in VCF will be removed. If NULL(default), no variants will be removed from the original VCF.

get.vaf.function

Optional. Only applicable when variant.caller is "unknown". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See GetMutectVAF as an example. If NULL(default) and variant.caller is "unknown", then VAF and read depth will be NAs.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A list containing the following objects:

- SBS: List of VCFs with only single base substitutions.
- DBS: List of VCFs with only doublet base substitutions.
- ID: List of VCFs with only small insertions and deletions.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

See Also

```
VCFsToCatalogs
```

Examples

ReadCatalog

Read catalog

Description

Read a catalog in standardized format from path.

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Usage

```
ReadCatalog(
  file,
  ref.genome = NULL,
  region = "unknown",
  catalog.type = "counts",
  strict = TRUE
)
```

Arguments

file Path to a catalog on disk in the standardized format.

ref.genome A ref.genome argument as described in ICAMS.

region A character string designating a genomic region; see as.catalog and

ICAMS.

catalog.type One of "counts", "density", "counts.signature", "density.signature".

strict If TRUE, do additional checks on the input, and stop if the checks fail.

Details

See also WriteCatalog

Value

A catalog as an S3 object; see as.catalog.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

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ReadStrelkaIDVCFs

Read Strelka ID (small insertion and deletion) VCF files

Description

Read Strelka ID (small insertion and deletion) VCF files

Usage

```
ReadStrelkaIDVCFs(files, names.of.VCFs = NULL)
```

Arguments

files

Character vector of file paths to the VCF files.

names.of.VCFs

Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

Value

A list of data frames containing data lines of the VCF files.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

See Also

```
StrelkaIDVCFFilesToCatalog
```

Examples

revc

Reverse complement every string in string.vec

Description

```
Based on reverseComplement. Handles IUPAC ambiguity codes but not "u" (uracil). (see <a href="https://en.wikipedia.org/wiki/Nucleic_acid_notation">https://en.wikipedia.org/wiki/Nucleic_acid_notation</a>).
```

Usage

```
revc(string.vec)
```

Arguments

string.vec A character vector.

Value

A character vector with the reverse complement of every string in string.vec.

Examples

```
revc("aTgc") # GCAT

# A vector and strings with ambiguity codes
revc(c("ATGC", "aTGc", "wnTCb")) # GCAT GCAT VGANW

## Not run:
revc("ACGU") # An error
## End(Not run)
```

StrelkaIDVCFFilesToCatalog

Create ID (small insertion and deletion) catalog from Strelka ID VCF files

Description

Create ID (small insertion and deletion) catalog from the Strelka ID VCFs specified by files

Usage

```
StrelkaIDVCFFilesToCatalog(
   files,
   ref.genome,
   region = "unknown",
   names.of.VCFs = NULL,
   flag.mismatches = 0,
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Strelka ID VCF files.

ref.genome A ref.genome argument as described in ICAMS.

region A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs Optional. Character vector of names of the VCF files. The order of names in

names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls VCFsToIDCatalogs

Value

A **list** of elements:

- catalog: The ID (small insertion and deletion) catalog with attributes added. See as.catalog for more details.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. A list of data frames which contain the original VCF's ID mutation rows with three additional columns seq.context.width, seq.context and ID.class added. The category assignment of each ID mutation in VCF can be obtained from ID.class column.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

StrelkaIDVCFFilesToCatalogAndPlotToPdf

Create ID (small insertion and deletion) catalog from Strelka ID VCF files and plot them to PDF

Description

Create ID (small insertion and deletion) catalog from the Strelka ID VCFs specified by files and plot them to PDF

Usage

```
StrelkaIDVCFFilesToCatalogAndPlotToPdf(
  ref.genome,
  region = "unknown",
  names.of.VCFs = NULL,
  output.file = "",
  flag.mismatches = 0,
 return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Strelka ID VCF files.

A ref. genome argument as described in ICAMS. ref.genome

region A character string designating a genomic region; see as. catalog and ICAMS.

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs

> names.of. VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

output.file Optional. The base name of the PDF file to be produced; the file is ending in

catID.pdf.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See

AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

 $This \ function \ calls \ StrelkaIDVCFFiles To Catalog \ and \ Plot Catalog To Pdf$

Value

A **list** of elements:

- catalog: The ID (small insertion and deletion) catalog with attributes added. See as.catalog
 for more details.
- discarded.variants: Non-NULL only if there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. A list of data frames which contain the original VCF's ID mutation rows with three additional columns seq.context.width, seq.context and ID.class added. The category assignment of each ID mutation in VCF can be obtained from ID.class column.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

StrelkaIDVCFFilesToZipFile

Create a zip file which contains ID (small insertion and deletion) catalog and plot PDF from Strelka ID VCF files

Description

Create ID (small insertion and deletion) catalog from the Strelka ID VCFs specified by dir, save the catalog as CSV file, plot it to PDF and generate a zip archive of all the output files.

Usage

```
StrelkaIDVCFFilesToZipFile(
    dir,
    zipfile,
    ref.genome,
    region = "unknown",
    names.of.VCFs = NULL,
    base.filename = "",
    flag.mismatches = 0,
    return.annotated.vcfs = FALSE,
    suppress.discarded.variants.warnings = TRUE
)
```

Arguments

dir Pathname of the directory which contains **only** the Strelka ID VCF files. Each

Strelka ID VCF must have a file extension ".vcf" (case insensitive) and share

the **same** ref.genome and region.

zipfile Pathname of the zip file to be created.

ref.genome A ref.genome argument as described in ICAMS.

region A character string designating a genomic region; see as . catalog and ICAMS.

names.of.VCFs Optional. Character vector of names of the VCF files. The order of names in

names.of.VCFs should match the order of VCFs listed in dir. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in dir and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

base.filename Optional. The base name of the CSV and PDF file to be produced; the file is

ending in catID.csv and catID.pdf respectively.

flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded variants will appear in the return value. See

AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls StrelkaIDVCFFilesToCatalog, PlotCatalogToPdf, WriteCatalog and zipr.

Value

A **list** of elements:

• catalog: The ID (small insertion and deletion) catalog with attributes added. See as.catalog for more details.

- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. A list of data frames which contain the original VCF's ID mutation rows with three additional columns seq.context.width, seq.context and ID.class added. The category assignment of each ID mutation in VCF can be obtained from ID.class column.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Examples

 ${\tt StrelkaSBSVCFFilesToCatalog}$

Create SBS and DBS catalogs from Strelka SBS VCF files

Description

Create 3 SBS catalogs (96, 192, 1536) and 3 DBS catalogs (78, 136, 144) from the Strelka SBS VCFs specified by files. The function will find and merge adjacent SBS pairs into DBS if their VAFs are very similar. The default threshold value for VAF is 0.02.

Usage

```
StrelkaSBSVCFFilesToCatalog(
   files,
   ref.genome,
   trans.ranges = NULL,
   region = "unknown",
   names.of.VCFs = NULL,
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Strelka SBS VCF files.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

- 1. BSgenome. Hsapiens. 1000 genomes. hs37d5
- 2. BSgenome. Hsapiens. UCSC. hg38
- 3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls VCFsToSBSCatalogs and VCFsToDBSCatalogs.

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

 ${\tt StrelkaSBSVCFFilesToCatalogAndPlotToPdf}$

Create SBS and DBS catalogs from Strelka SBS VCF files and plot them to PDF

Description

Create 3 SBS catalogs (96, 192, 1536) and 3 DBS catalogs (78, 136, 144) from the Strelka SBS VCFs specified by files and plot them to PDF. The function will find and merge adjacent SBS pairs into DBS if their VAFs are very similar. The default threshold value for VAF is 0.02.

Usage

```
StrelkaSBSVCFFilesToCatalogAndPlotToPdf(
  files,
  ref.genome,
  trans.ranges = NULL,
  region = "unknown",
  names.of.VCFs = NULL,
  output.file = "",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

files Character vector of file paths to the Strelka SBS VCF files.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome. Hsapiens. 1000 genomes. hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs Optional. Character vector of names of the VCF files. The order of names in

names. of . VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

output.file Optional. The base name of the PDF files to be produced; multiple files will be

generated, each ending in x.pdf, where x indicates the type of catalog plotted in the file.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

 $This \ function \ calls \ Strelka SBSVCFFiles To Catalog \ and \ Plot Catalog To Pdf$

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

StrelkaSBSVCFFilesToZipFile

Create a zip file which contains catalogs and plot PDFs from Strelka SBS VCF files

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) from the Strelka SBS VCFs specified by dir, save the catalogs as CSV files, plot them to PDF and generate a zip archive of all the output files. The function will find and merge adjacent SBS pairs into DBS if their VAFs are very similar. The default threshold value for VAF is 0.02.

Usage

```
StrelkaSBSVCFFilesToZipFile(
   dir,
   zipfile,
   ref.genome,
   trans.ranges = NULL,
   region = "unknown",
   names.of.VCFs = NULL,
   base.filename = "",
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE
)
```

Arguments

dir Pathname of the directory which contains **only** the Strelka SBS VCF files. Each

Strelka SBS VCF must have a file extension ".vcf" (case insensitive) and share

the **same** ref.genome and region.

zipfile Pathname of the zip file to be created.

ref.genome A ref.genome argument as described in ICAMS.

trans.ranges Optional. If ref. genome specifies one of the BSgenome object

1. BSgenome. Hsapiens. 1000 genomes. hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information

region A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCFs listed in dir. If NULL(default),

this function will remove all of the path up to and including the last path separator (if any) in dir and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

base.filename Optional. The base name of the CSV and PDF files to be produced; multiple

files will be generated, each ending in $x.\operatorname{csv}$ or $x.\operatorname{pdf}$, where x indicates the

type of catalog.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls StrelkaSBSVCFFilesToCatalog, PlotCatalogToPdf, WriteCatalog and zipr.

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class,
 DBS136.class and DBS144.class showing the mutation class for each DBS variant.

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If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions.

Comments

```
To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <- custom. abundance.
```

Examples

TranscriptRanges

Transcript ranges data

Description

Transcript ranges and strand information for a particular reference genome.

Usage

```
trans.ranges.GRCh37
trans.ranges.GRCh38
trans.ranges.GRCm38
```

Format

A data.table which contains transcript range and strand information for a particular reference genome. colnames are chrom, start, end, strand, Ensembl.gene.ID, gene.symbol. It uses one-based coordinates.

An object of class data.table (inherits from data.frame) with 19083 rows and 6 columns.

An object of class data.table (inherits from data.frame) with 19096 rows and 6 columns.

An object of class data.table (inherits from data.frame) with 20325 rows and 6 columns.

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Details

This information is needed to generate catalogs that depend on transcriptional strand information, for example catalogs of class SBS192Catalog.

```
trans.ranges.GRCh37: Human GRCh37. trans.ranges.GRCh38: Human GRCh38. trans.ranges.GRCm38: Mouse GRCm38.
```

For these two tables, only genes that are associated with a CCDS ID are kept for transcriptional strand bias analysis.

```
This information is needed for StrelkaSBSVCFFilesToCatalog,
StrelkaSBSVCFFilesToCatalogAndPlotToPdf, MutectVCFFilesToCatalog,
MutectVCFFilesToCatalogAndPlotToPdf, VCFsToSBSCatalogs and VCFsToDBSCatalogs.
```

Source

```
ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_human/release_30/GRCh37_mapping/
gencode.v30lift37.annotation.gff3.gz
ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_human/release_30/gencode.v30.annotation.
gff3.gz
ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_mouse/release_M21/gencode.vM21.
annotation.gff3.gz
```

Examples

```
trans.ranges.GRCh37
# chrom
        start
                   end strand Ensembl.gene.ID gene.symbol
#
         65419 71585 + ENSG00000186092
                                                 OR4F5
    1
                          + ENSG00000235249
#
       367640 368634
                                                 OR4F29
    1
#
    1
       621059 622053
                          - ENSG00000284662
                                                 OR4F16
    1
        859308
                879961
                           + ENSG00000187634
                                                 SAMD11
       879583
                894689
                           - ENSG00000188976
                                                 NOC2L
           . . .
                   . . .
                                                    . . .
```

TransformCatalog

Transform between counts and density spectrum catalogs and counts and density signature catalogs

Description

Transform between counts and density spectrum catalogs and counts and density signature catalogs

Usage

```
TransformCatalog(
  catalog,
  target.ref.genome = NULL,
  target.region = NULL,
  target.catalog.type = NULL,
  target.abundance = NULL
)
```

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Arguments

catalog

An SBS or DBS catalog as described in ICAMS; must **not** be an ID (small insertion and deletion) catalog.

target.ref.genome

A ref.genome argument as described in ICAMS. If NULL, then defaults to the ref.genome attribute of catalog.

target.region

A region argument; see as.catalog and ICAMS. If NULL, then defaults to the region attribute of catalog.

target.catalog.type

A character string acting as a catalog type identifier, one of "counts", "density", "counts.signature", "density.signature"; see as.catalog. If NULL, then defaults to the catalog. type attribute of catalog.

target.abundance

A vector of counts, one for each source K-mer for mutations (e.g. for strandagnostic single nucleotide substitutions in trinucleotide – i.e. 3-mer – context, one count each for ACA, ACC, ACG, ... TTT). See all abundance. If NULL, the function tries to infer target abundance from the class of catalog and the value of the target.ref.genome, target.region, and target.catalog.type. If the target abundance can be inferred and is different from a supplied non-NULL value of target abundance, raise an error.

Details

Only the following transformations are legal:

- counts -> counts (deprecated, generates a warning; we strongly suggest that you work with densities if comparing spectra or signatures generated from data with different underlying abundances.)
- 2. counts -> density
- 3. counts -> (counts.signature,density.signature)
- 4. density -> counts (the semantics are to infer the genome-wide or exome-wide counts based on the densities)
- 5. density -> density (a null operation, generates a warning)
- 6. density -> (counts.signature, density.signature)
- 7. counts.signature -> counts.signature (used to transform between the source abundance and target.abundance)
- 8. counts.signature -> density.signature
- 9. counts.signature -> (counts, density) (generates an error)
- 10. density.signature -> density.signature (a null operation, generates a warning)
- 11. density.signature -> counts.signature
- 12. density.signature -> (counts, density) (generates an error)

Value

A catalog as defined in ICAMS.

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Rationale

The TransformCatalog function transforms catalogs of mutational spectra or signatures to account for differing abundances of the source sequence of the mutations in the genome.

For example, mutations from ACG are much rarer in the human genome than mutations from ACC simply because CG dinucleotides are rare in the genome. Consequently, there are two possible representations of mutational spectra or signatures. One representation is based on mutation counts as observed in a given genome or exome, and this approach is widely used, as, for example, at https://cancer.sanger.ac.uk/cosmic/signatures, which presents signatures based on observed mutation counts in the human genome. We call these "counts-based spectra" or "counts-based signatures".

Alternatively, mutational spectra or signatures can be represented as mutations per source sequence, for example the number of ACT > AGT mutations occurring at all ACT 3-mers in a genome. We call these "density-based spectra" or "density-based signatures".

This function can also transform spectra based on observed genome-wide counts to "density"-based catalogs. In density-based catalogs mutations are expressed as mutations per source sequences. For example, a density-based catalog represents the proportion of ACCs mutated to ATCs, the proportion of ACGs mutated to ATGs, etc. This is different from counts-based mutational spectra catalogs, which contain the number of ACC > ATC mutations, the number of ACG > ATG mutations, etc.

This function can also transform observed-count based spectra or signatures from genome to exome based counts, or between different species (since the abundances of source sequences vary between genome and exome and between species).

Examples

VCFsToCatalogs

Create SBS, DBS and Indel catalogs from VCFs

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the Mutect VCFs specified by files

Usage

```
VCFsToCatalogs(
  files,
  ref.genome,
  variant.caller = "unknown",
```

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```
trans.ranges = NULL,
region = "unknown",
names.of.VCFs = NULL,
tumor.col.names = NA,
filter.status = NULL,
get.vaf.function = NULL,
return.annotated.vcfs = FALSE,
suppress.discarded.variants.warnings = TRUE)
```

Arguments

files Character vector of file paths to the VCF files.

ref.genome A ref.genome argument as described in ICAMS.

 $variant. \, caller \ \ \, Name \, of \, the \, variant \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, be a constant of the variant \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, mutect \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, the \, variant \, caller \, that \, produces \, the \, VCF, \, can \, be \, either \, strelka, \, the \, variant \, caller \, t$

or freebayes. This information is needed to calculate the VAFs (variant allele frequencies). If "unknown" (default) and get.vaf.function is NULL, then

VAF and read depth will be NAs.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome. Hsapiens. 1000genomes. hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information

region

A character string designating a genomic region; see as. catalog and ICAMS.

 ${\tt names.of.VCFs}$

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Only applicable to **Mutect** VCFs. Character vector of column names in **Mutect** VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of **Mutect** VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the **Mutect** VCFs to calculate VAFs. See GetMutectVAF for more details

filter.status

The status indicating a variant has passed all filters. An example would be "PASS". Variants which don't have the specified filter.status in the FILTER column in VCF will be removed. If NULL(default), no variants will be removed from the original VCF.

get.vaf.function

Optional. Only applicable when variant.caller is "unknown". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See GetMutectVAF as an example. If NULL(default) and variant.caller is "unknown", then VAF and read depth will be NAs.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

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suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls VCFsToSBSCatalogs, VCFsToDBSCatalogs and VCFsToIDCatalogs

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID. class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

VCFsToCatalogsAndPlotToPdf

Create SBS, DBS and Indel catalogs from VCFs and plot them to PDF

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the VCFs specified by files and plot them to PDF

Usage

```
VCFsToCatalogsAndPlotToPdf(
   files,
   output.dir,
   ref.genome,
   variant.caller = "unknown",
   trans.ranges = NULL,
   region = "unknown",
   names.of.VCFs = NULL,
   tumor.col.names = NA,
   filter.status = NULL,
   get.vaf.function = NULL,
   base.filename = "",
   return.annotated.vcfs = FALSE,
   suppress.discarded.variants.warnings = TRUE)
```

Arguments

files Character vector of file paths to the VCF files.

output.dir The directory where the PDF files will be saved.

ref.genome A ref.genome argument as described in ICAMS.

variant.caller Name of the variant caller that produces the VCF, can be either strelka, mutect or freebayes. This information is needed to calculate the VAFs (variant allele frequencies). If "unknown"(default) and get.vaf.function is NULL, then VAF and read depth will be NAs.

trans.ranges Optional. If ref.genome specifies one of the BSgenome object

1. BSgenome.Hsapiens.1000genomes.hs37d5

2. BSgenome.Hsapiens.UCSC.hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as.catalog and ICAMS.

names.of.VCFs

Optional. Character vector of names of the VCF files. The order of names in names.of.VCFs should match the order of VCF file paths in files. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in files and file paths without extensions (and the leading dot) will be used as the names of the VCF files.

tumor.col.names

Optional. Only applicable to **Mutect** VCFs. Character vector of column names in **Mutect** VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of **Mutect** VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the **Mutect** VCFs to calculate VAFs. See GetMutectVAF for more details.

filter.status

The status indicating a variant has passed all filters. An example would be "PASS". Variants which don't have the specified filter.status in the FILTER column in VCF will be removed. If NULL(default), no variants will be removed from the original VCF.

get.vaf.function

Optional. Only applicable when variant.caller is "unknown". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See GetMutectVAF as an example. If NULL(default) and variant.caller is "unknown", then VAF and read depth will be NAs.

base.filename

Optional. The base name of the PDF files to be produced; multiple files will be generated, each ending in x.pdf, where x indicates the type of catalog plotted in the file.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Details

This function calls VCFsToCatalogs and PlotCatalogToPdf

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class,
 DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID.class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Examples

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VCFsToDBSCatalogs

Create DBS catalogs from VCFs

Description

Create a list of 3 catalogs (one each for DBS78, DBS144 and DBS136) out of the contents in list.of.DBS.vcfs. The VCFs must not contain any type of mutation other then DBSs.

Usage

```
VCFsToDBSCatalogs(
  list.of.DBS.vcfs,
  ref.genome,
  trans.ranges = NULL,
  region = "unknown",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

list.of.DBS.vcfs

List of in-memory data frames of pure DBS mutations – no SBS or 3+BS mutations. The list names will be the sample ids in the output catalog.

ref.genome

A ref. genome argument as described in ICAMS.

trans.ranges

Optional. If ref. genome specifies one of the BSgenome object

- 1. BSgenome. Hsapiens. 1000 genomes. hs37d5
- 2. BSgenome.Hsapiens.UCSC.hg38
- 3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as.catalog and ICAMS.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A list containing the following objects:

- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

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annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class, DBS136.class and DBS144.class showing the mutation class for each DBS variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

Comments

```
To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.
```

Note

DBS 144 catalog only contains mutations in transcribed regions.

Examples

VCFsToIDCatalogs

Create ID (small insertion and deletion) catalog from ID VCFs

Description

Create ID (small insertion and deletion) catalog from ID VCFs

Usage

```
VCFsToIDCatalogs(
  list.of.vcfs,
  ref.genome,
  region = "unknown",
  flag.mismatches = 0,
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

```
list.of.vcfs List of in-memory ID VCFs. The list names will be the sample ids in the output catalog.

ref.genome A ref.genome argument as described in ICAMS.

region A character string acting as a region identifier, one of "genome", "exome".
```

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flag.mismatches

Deprecated. If there are ID variants whose REF do not match the extracted sequence from ref.genome, the function will automatically discard these variants and an element discarded.variants will appear in the return value. See AnnotateIDVCF for more details.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A **list** of elements:

- catalog: The ID (small insertion and deletion) catalog with attributes added. See as.catalog for details.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. A list of data frames which contain the original VCF's ID mutation rows with three additional columns seq.context.width, seq.context and ID.class added. The category assignment of each ID mutation in VCF can be obtained from ID.class column.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACAC, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Examples

VCFsToSBSCatalogs 61

VCFsToSBSCatalogs

Create SBS catalogs from SBS VCFs

Description

Create a list of 3 catalogs (one each for 96, 192, 1536) out of the contents in list.of.SBS.vcfs. The SBS VCFs must not contain DBSs, indels, or other types of mutations.

Usage

```
VCFsToSBSCatalogs(
  list.of.SBS.vcfs,
  ref.genome,
  trans.ranges = NULL,
  region = "unknown",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

Arguments

list.of.SBS.vcfs

List of in-memory data frames of pure SBS mutations – no DBS or 3+BS mutations. The list names will be the sample ids in the output catalog.

ref.genome

A ref. genome argument as described in ICAMS.

trans.ranges

Optional. If ref. genome specifies one of the BSgenome object

- 1. BSgenome. Hsapiens. 1000 genomes. hs37d5
- 2. BSgenome.Hsapiens.UCSC.hg38
- 3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

region

A character string designating a genomic region; see as.catalog and ICAMS.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.

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• annotated.vcfs: **Non-NULL only if** return.annotated.vcfs = TRUE. SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

Note

SBS 192 catalogs only contain mutations in transcribed regions.

Examples

VCFsToZipFile

Create a zip file which contains catalogs and plot PDFs from VCFs

Description

Create 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and Indel catalog from the VCFs specified by dir, save the catalogs as CSV files, plot them to PDF and generate a zip archive of all the output files.

Usage

```
VCFsToZipFile(
    dir,
    zipfile,
    ref.genome,
    variant.caller = "unknown",
    trans.ranges = NULL,
    region = "unknown",
    names.of.VCFs = NULL,
    tumor.col.names = NA,
    filter.status = NULL,
    get.vaf.function = NULL,
    base.filename = "",
    return.annotated.vcfs = FALSE,
    suppress.discarded.variants.warnings = TRUE)
```

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Arguments

dir Pathname of the directory which contains VCFs that come from the same variant

caller. Each VCF must have a file extension ".vcf" (case insensitive) and share

the same ref. genome and region.

zipfile Pathname of the zip file to be created.

ref.genome A ref. genome argument as described in ICAMS.

variant.caller Name of the variant caller that produces the VCF, can be either strelka, mutect

> or freebayes. This information is needed to calculate the VAFs (variant allele frequencies). If "unknown" (default) and get.vaf.function is NULL, then

VAF and read depth will be NAs.

Optional. If ref. genome specifies one of the BSgenome object trans.ranges

1. BSgenome. Hsapiens. 1000 genomes. hs37d5

2. BSgenome. Hsapiens. UCSC. hg38

3. BSgenome.Mmusculus.UCSC.mm10

then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to TranscriptRanges for more details. If is.null(trans.ranges) do not add transcript range information.

A character string designating a genomic region; see as.catalog and ICAMS. region

> Optional. Character vector of names of the VCF files. The order of names in names. of . VCFs should match the order of VCFs listed in dir. If NULL(default), this function will remove all of the path up to and including the last path separator (if any) in dir and file paths without extensions (and the leading dot) will

be used as the names of the VCF files.

tumor.col.names

Optional. Only applicable to **Mutect** VCFs. Character vector of column names in **Mutect** VCFs which contain the tumor sample information. The order of names in tumor.col.names should match the order of Mutect VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the Mutect VCFs to calculate VAFs. See GetMutectVAF for

more details.

The status indicating a variant has passed all filters. An example would be filter.status "PASS". Variants which don't have the specified filter.status in the FILTER

column in VCF will be removed. If NULL(default), no variants will be removed

from the original VCF.

get.vaf.function

Optional. Only applicable when variant.caller is "unknown". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See GetMutectVAF as an example. If NULL(default) and variant.caller

is "unknown", then VAF and read depth will be NAs.

base.filename Optional. The base name of the CSV and PDF files to be produced; multiple

files will be generated, each ending in x.csv or x.pdf, where x indicates the

type of catalog.

return.annotated.vcfs

Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.

suppress.discarded.variants.warnings

Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

names.of.VCFs

64 VCFsToZipFile

Details

This function calls VCFsToCatalogs, PlotCatalogToPdf, WriteCatalog and zipr.

Value

A list containing the following objects:

- catSBS96, catSBS192, catSBS1536: Matrix of 3 SBS catalogs (one each for 96, 192, and 1536).
- catDBS78, catDBS136, catDBS144: Matrix of 3 DBS catalogs (one each for 78, 136, and 144).
- catID: Matrix of ID (small insertion and deletion) catalog.
- discarded.variants: **Non-NULL only if** there are variants that were excluded from the analysis. See the added extra column discarded.reason for more details.
- annotated.vcfs: Non-NULL only if return.annotated.vcfs = TRUE. A list of elements:
 - SBS: SBS VCF annotated by AnnotateSBSVCF with three new columns SBS96.class, SBS192.class and SBS1536.class showing the mutation class for each SBS variant.
 - DBS: DBS VCF annotated by AnnotateDBSVCF with three new columns DBS78.class,
 DBS136.class and DBS144.class showing the mutation class for each DBS variant.
 - ID: ID VCF annotated by AnnotateIDVCF with one new column ID.class showing the mutation class for each ID variant.

If trans.ranges is not provided by user and cannot be inferred by ICAMS, SBS 192 and DBS 144 catalog will not be generated. Each catalog has attributes added. See as.catalog for more details.

ID classification

See https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_ 2017_12_08.xlsx for additional information on ID (small insertion and deletion) mutation classification.

See the documentation for Canonicalize1Del which first handles deletions in homopolymers, then handles deletions in simple repeats with longer repeat units, (e.g. CACACACA, see FindMaxRepeatDel), and if the deletion is not in a simple repeat, looks for microhomology (see FindDelMH).

See the code for unexported function CanonicalizeID and the functions it calls for handling of insertions.

Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

Comments

To add or change attributes of the catalog, you can use function attr. For example, attr(catalog, "abundance") <-custom.abundance.

WriteCatalog 65

Examples

WriteCatalog

Write a catalog

Description

Write a catalog to a file.

Usage

```
WriteCatalog(catalog, file, strict = TRUE)
```

Arguments

catalog A catalog as defined in ICAMS; see also as.catalog.

file The path to the file to be created.

strict If TRUE, do additional checks on the input, and stop if the checks fail.

Details

See also ReadCatalog.

Note

In ID (small insertion and deletion) catalogs, deletion repeat sizes range from 0 to 5+, but for plotting and end-user documentation deletion repeat sizes range from 1 to 6+.

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