

# Package ‘ICAMS’

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**Type** Package

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

**Version** 3.0.0.9007

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**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, <[doi:10.1101/gr.230219.117](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 <[doi:10.1101/gr.255620.119](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" (i.e. representation as mutations per megabase) mutational spectra or signatures.

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**URL** <https://github.com/steverozen/ICAMS>

**BugReports** <https://github.com/steverozen/ICAMS/issues>

**Encoding** UTF-8

**LazyData** true

**Language** en-US

**biocViews**

**Imports** Biostrings,  
BSgenome,  
data.table,  
dplyr,  
GenomeInfoDb,  
GenomicRanges,  
graphics,  
grDevices,  
IRanges,

lifecycle,  
RColorBrewer,  
stats,  
stringi,  
utils,  
zip

**Depends** R ( $\geq 3.5$ ),

**RoxygenNote** 7.1.1

**Suggests** BSgenome.Hsapiens.1000genomes.hs37d5,

BSgenome.Hsapiens.UCSC.hg38,  
BSgenome.Mmusculus.UCSC.mm10,  
ggplot2,  
reshape2,  
rlang,  
testthat

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all.abundance	<i>K-mer abundances</i>
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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.
```



---

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

---

## Description

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

## Usage

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

## Arguments

ID.vcf	An in-memory ID (insertion/deletion) VCF as a <code>data.frame</code> . 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 <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
flag.mismatches	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants. See element <code>discarded.variants</code> 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

```
file <- c(system.file("extdata/Strelka-ID-vcf/",
                     "Strelka.ID.GRCh37.s1.vcf",
                     package = "ICAMS"))
ID.vcf <- ReadStrelkaIDVCFs(file)[[1]]
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  list <- AnnotateIDVCF(ID.vcf, ref.genome = "hg19")
  annotated.ID.vcf <- list$annotated.vcf}
```

---

AnnotateSBSVCF	<i>Add sequence context and transcript information to an in-memory SBS VCF</i>
----------------	--

---

## Description

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

## Usage

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

## Arguments

SBS.vcf	An in-memory SBS VCF as a data.frame.
ref.genome	A ref.genome argument as described in <a href="#">ICAMS</a> .
trans.ranges	Optional. If ref.genome specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. BSgenome.Hsapiens.1000genomes.hs37d5</li> <li>2. BSgenome.Hsapiens.UCSC.hg38</li> <li>3. BSgenome.Mmusculus.UCSC.mm10</li> </ol> then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to <a href="#">TranscriptRanges</a> for more details. If is.null(trans.ranges) do not add transcript range information.
name.of.VCF	Name of the VCF file.

## 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

```
file <- c(system.file("extdata/Strelka-SBS-vcf",
                     "Strelka.SBS.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadAndSplitStrelkaSBSVCFs(file)
SBS.vcf <- list.of.vcfs$SBS.vcfs[[1]]
```

```
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  annotated.SBS.vcf <- AnnotateSBSVCF(SBS.vcf, ref.genome = "hg19",
                                     trans.ranges = trans.ranges.GRCh37)}
}
```

as.catalog

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

## Description

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

## Usage

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

## 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 then this argument must have rownames to denote the mutation types. See <a href="#">CatalogRowOrder</a> for more details. |
| ref.genome     | A ref.genome argument as described in <a href="#">ICAMS</a> .   |
| region         | A character string designating a region, one of genome, transcript, exome, unknown; see <a href="#">ICAMS</a> . If the catalog type is a stranded catalog type (SBS192 or DBS144), region = "genome" will be silently converted to "transcript".  |
| 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 <a href="#">ICAMS</a> . The argument abundance should contain the counts of different source sequences for mutations in the same format as the numeric vectors in <a href="#">all.abundance</a> .                                |
| 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, <b>be sure the order of rows is correct</b> .   |

## Value

A catalog as described in [ICAMS](#).

## Examples

```
# Create an SBS96 catalog with all mutation counts equal to 1.
object <- matrix(1, nrow = 96, ncol = 1,
                 dimnames = list(catalog.row.order$SBS96))
catSBS96 <- as.catalog(object)
```

---

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.

## Details

See [https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7\\_indel\\_classification\\_2017\\_12\\_08.xlsx](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 [FindDeIMH](#)).

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 [FindDeIMH](#) 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	<i>Standard order of row names in a catalog</i>
-----------------	---

---

## 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
```

## Format

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

An object of class `list` of length 8.

## ID classification

See [https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7\\_indel\\_classification\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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.
```

---

CollapseCatalog	<i>"Collapse" a catalog</i>
-----------------	-----------------------------

---

### 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](#).

### Value

A catalog as defined in [ICAMS](#).

### Examples

```
# Create an SBS192 catalog and collapse it to an SBS96 catalog
object <- matrix(1, nrow = 192, ncol = 1,
                 dimnames = list(catalog.row.order$SBS192))
catSBS192 <- as.catalog(object, region = "transcript")
catSBS96 <- Collapse192CatalogTo96(catSBS192)
```

---

FindDelMH	<i>Return the length of microhomology at a deletion</i>
-----------	---

---

### 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
CCGATCTTGATCAA

```

=>

```

....
GGCTAG      TT
CC      GATCAA
      ....

```

=>

```

GGCTAGTT
CCGATCAA

```

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

```

GGC-----TAGTT  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
GACTA----GTT 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.**

### 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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**

```
# GAGAGG[CTAGAA]CTAGTT
#      ----  ----
FindDelMH("GGAGAGGCTAGAACTAGTTAAAAA", "CTAGAA", 8, trace = 0) # 4

# A cryptic repeat
#
# TAAATTATTTATTAATTTATTG
# TAAATTA----TTAATTTATTG = TAAATTATTAATTTATTG
#
# equivalent to
#
# TAAATTATTTATTAATTTATTG
# TAAAT----TATTAATTTATTG = TAAATTATTAATTTATTG
#
# and
#
# TAAATTATTTATTAATTTATTG
# TAAA----TTATTAATTTATTG = TAAATTATTAATTTATTG

FindDelMH("TAAATTATTTATTAATTTATTG", "TTTA", 8, warn.cryptic = FALSE) # -1
```

---

FindMaxRepeatDel	<i>Return the number of repeat units in which a deletion is embedded</i>
------------------	--

---

**Description**

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

**Usage**

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

**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 note that the return value does not include the `rep.unit.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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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("xyACACzt", "AC", 3) # 1
FindMaxRepeatDel("xyACACzt", "CA", 4) # 0
```

---

GeneExpressionData	<i>Example gene expression data from two cell lines</i>
--------------------	---

---

### Description

This data is designed to be used as an example in function [PlotTransBiasGeneExp](#) and [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
# ENSG000000000003 TSPAN6 6007 33.922648455
# ENSG000000000005 TNMD 0 0.000000000
# ENSG000000000419 DPM1 4441 61.669371091
# ENSG000000000457 SCYL3 1368 3.334619195
# ENSG000000000460 C1orf112 916 2.416263423
# ...
```

---

GeneratePlotPFMmatrix *Generate PFMmatrix (Position Frequency Matrix) from a given list of sequences*

---

**Description**

Generate PFMmatrix (Position Frequency Matrix) from a given list of sequences

**Usage**

```
GeneratePlotPFMmatrix(
  sequences,
  indel.class,
  flank.length = 5,
  plot.dir = NULL,
  plot.title = NULL
)
```

**Arguments**

<code>sequences</code>	A list of strings returned from <a href="#">SymmetricalContextsFor1BPIndel</a> .
<code>indel.class</code>	A single character string that denotes a 1 base pair insertion or deletion, as taken from <code>ICAMS::catalog.row.order\$ID</code> . Insertions or deletions into or from 5+ base-pair homopolymers are not supported.
<code>flank.length</code>	The length of flanking bases around the position or homopolymer targeted by the indel.
<code>plot.dir</code>	If provided, make a dot-line plot for PFMmatrix.
<code>plot.title</code>	The title of the dot-line plot

**Value**

A matrix recording the frequency of each base (A, C, G, T) on each position of the sequence.

## Examples

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
split.vcfs <- ReadAndSplitVCFs(file, variant.caller = "mutect")
ID.catalog <- VCFsToIDCatalogs(list.of.vcfs = split.vcfs$ID,
                              ref.genome = "hg19",
                              region = "genome",
                              return.annotated.vcfs = TRUE)
annotated.vcf <- ID.catalog$annotated.vcfs$Mutect.GRCh37.s1
extended.seq.contexts <-
  SymmetricalContextsFor1BPIndel(annotated.vcf = annotated.vcf,
                                indel.class = "DEL:T:1:0")
GeneratePlotPFMatrix(sequences = extended.seq.contexts,
                     indel.class = "DEL:T:1:0",
                     plot.dir = file.path(tempdir(), "test.pdf"),
                     plot.title = "Deletion of 1T from 1T")
```

---

GetVAF	<i>Extract the VAFs (variant allele frequencies) and read depth information from a VCF file</i>
--------	---

---

## Description

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

## Usage

```
GetStrelkaVAF(vcf, name.of.VCF = NULL)

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

GetFreebayesVAF(vcf, name.of.VCF = NULL)

GetPCAWGConsensusVAF(vcf, mc.cores = 1)
```

## Arguments

<code>vcf</code>	An in-memory VCF data frame.
<code>name.of.VCF</code>	Name of the VCF file.
<code>tumor.col.name</code>	Optional. Only applicable to <b>Mutect</b> VCF. Name or index of the column in <b>Mutect</b> VCF which contains the tumor sample information. It <b>must</b> have quotation marks if specifying the column name. If <code>tumor.col.name</code> is equal to NA(default), this function will use the 10th column to calculate VAFs.
<code>mc.cores</code>	The number of cores to use. Not available on Windows unless <code>mc.cores = 1</code> .

## Value

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



**Note**

[GetPCAWGConsensusVAF](#) is analogous to [GetMutectVAF](#), calculating VAF and read depth from PCAWG7 consensus vcfs

**Examples**

```
file <- c(system.file("extdata/Strelka-SBS-vcf",
                     "Strelka.SBS.GRCh37.s1.vcf",
                     package = "ICAMS"))
MakeDataFrameFromVCF <- getFromNamespace("MakeDataFrameFromVCF", "ICAMS")
df <- MakeDataFrameFromVCF(file)
df1 <- GetStrelkaVAF(df)
```

HaplotypePlot

*Generate Haplotype plot from a given list of sequences***Description**

Generate Haplotype plot from a given list of sequences

**Usage**

```
HaplotypePlot(
  sequences,
  indel.class,
  flank.length = 5,
  title = "Haplotype Plot"
)
```

**Arguments**

sequences	A list of strings returned from <a href="#">SymmetricalContextsFor1BPIndel</a> .
indel.class	A single character string that denotes a 1 base pair insertion or deletion, as taken from <code>ICAMS::catalog.row.order\$ID</code> . Insertions or deletions into or from 5+ base-pair homopolymers are not supported.
flank.length	The length of flanking bases around the position or homopolymer targeted by the indel.
title	The title of the haplotype plot

**Value**

A ggplot2 object

**Examples**

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
split.vcfs <- ReadAndSplitVCFs(file, variant.caller = "mutect")
ID.catalog <- VCFsToIDCatalogs(list.of.vcfs = split.vcfs$ID,
                              ref.genome = "hg19",
```

```

        region = "genome",
        return.annotated.vcfs = TRUE)
annotated.vcf <- ID.catalog$annotated.vcfs$Mutect.GRCh37.s1
extended.seq.contexts <-
  SymmetricalContextsFor1BPIndel(annotated.vcf = annotated.vcf,
    indel.class = "INS:T:1:4")
ggplot.object <- HaplotypePlot(sequences = extended.seq.contexts,
  indel.class = "INS:T:1:4",
  title = "Deletion of 1T from 4Ts")
plot(ggplot.object)

```

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.

## Details

"ICAMS" can read in VCFs generated by Strelka, Mutect or other variant callers, 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), doublet 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 (see below), 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 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 [VCFsToCatalogs](#), [VCFsToZipFile](#), etc.), then use [as.catalog](#).

### Creating catalogs from variant call files (VCF files)

- [VCFsToCatalogs](#) creates 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and ID (small insertions and deletions) catalog from the VCFs.

### Plotting catalogs

- [PlotCatalog](#) function plots mutational spectra for **one** sample or plot **one** mutational signature.
- [PlotCatalogToPdf](#) function plots catalogs of mutational spectra or of mutational signatures to a PDF file.

### Wrapper function to create catalogs from VCFs and plot the catalogs to PDF files

- [VCFsToCatalogsAndPlotToPdf](#) creates all types of SBS, DBS and ID catalogs from VCFs and plots the catalogs.

### Wrapper function 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.

### 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

- [WriteCatalog](#) function writes a catalog to a file.

### Reading catalogs

- [ReadCatalog](#) function reads a file that contains a catalog in standardized format.

### Transforming catalogs

[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/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**[CollapseCatalog](#) function

1. Takes 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. Collapses 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. [all.abundance](#) The counts of different source sequences for mutations.
4. [GeneExpressionData](#) Example gene expression data from two cell lines.

---

MutectVCFFilesToCatalog

**[Deprecated, use `VCFsToCatalogs(variant.caller = "mutect")` instead]** Create SBS, DBS and Indel catalogs from Mutect VCF files

---

**Description**

**[Deprecated, use `VCFsToCatalogs(variant.caller = "mutect")` instead]** 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**

<code>files</code>	Character vector of file paths to the Mutect VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> </ol>

	<ol style="list-style-type: none"> <li>2. BSgenome.Hsapiens.UCSC.hg38</li> <li>3. BSgenome.Mmusculus.UCSC.mm10</li> </ol>
	then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Vector of column names or column indices in VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of VCFs specified in <code>files</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## 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 insertions and deletions) 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 [AnnotateSBSCVCF](#) with three new columns `SBS96.class`, `SBS192.class` and `SBS1536.class` showing the mutation class for each SBS variant.
  - DBS: DBS VCF annotated by [AnnotateDBSCVCF](#) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <- MutectVCFFilesToCatalog(file, ref.genome = "hg19",
                                     trans.ranges = trans.ranges.GRCh37,
                                     region = "genome")}
```

---

MutectVCFFilesToCatalogAndPlotToPdf

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "mutect")` instead]** Create SBS, DBS and Indel catalogs from Mutect VCF files and plot them to PDF

---

## Description

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "mutect")` instead]** 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

**Usage**

```
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**

<code>files</code>	Character vector of file paths to the Mutect VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li><code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li><code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li><code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Vector of column names or column indices in VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of VCFs specified in <code>files</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>output.file</code>	Optional. The base name of the PDF files to be produced; multiple files will be generated, each ending in <code>x.pdf</code> , where <code>x</code> indicates the type of catalog plotted in the file.
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .



`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 insertions and deletions) 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.

## Note

SBS 192 and DBS 144 catalogs include only mutations in transcribed regions. In ID (small insertions and deletions) 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`.

## ID classification

See [https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7\\_indel\\_classification\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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**

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <-
    MutectVCFFilesToCatalogAndPlotToPdf(file, ref.genome = "hg19",
                                         trans.ranges = trans.ranges.GRCh37,
                                         region = "genome",
                                         output.file =
                                         file.path(tempdir(), "Mutect"))}
```

---

MutectVCFFilesToZipFile

**[Deprecated, use VCFsToZipFile(variant.caller = "mutect") instead]** *Create a zip file which contains catalogs and plot PDFs from Mutect VCF files*

---

**Description**

**[Deprecated, use VCFsToZipFile(variant.caller = "mutect") instead]** 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**

<code>dir</code>	Pathname of the directory which contains <b>only</b> the Mutect VCF files. Each Mutect VCF <b>must</b> have a file extension ".vcf" (case insensitive) and share the <b>same</b> <code>ref.genome</code> and region.
<code>zipfile</code>	Pathname of the zip file to be created.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> </ol>

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.

<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCFs listed in <code>dir</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>dir</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Vector of column names or column indices in VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of VCFs listed in <code>dir</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>base.filename</code>	Optional. The base name of the CSV and PDF files to be produced; multiple files will be generated, each ending in <code>x.csv</code> or <code>x.pdf</code> , where <code>x</code> indicates the type of catalog.
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## Details

This function calls [MutectVCFFilesToCatalog](#), [PlotCatalogToPdf](#), [WriteCatalog](#) and `zip::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 insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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

```
dir <- c(system.file("extdata/Mutect-vcf",
  package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <-
    MutectVCFFilesToZipFile(dir,
      zipfile = file.path(tempdir(), "test.zip"),
      ref.genome = "hg19",
      trans.ranges = trans.ranges.GRCh37,
      region = "genome",
      base.filename = "Mutect")
  unlink(file.path(tempdir(), "test.zip"))
}
```

PlotCatalog

*Plot **one** spectrum or signature***Description**

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

**Usage**

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

**Arguments**

catalog	A catalog as defined in <a href="#">ICAMS</a> with attributes added. See <a href="#">as.catalog</a> for more details. catalog can also be a numeric matrix, numeric data.frame, or a vector denoting the mutation <b>counts</b> , but <b>must</b> be in the correct row order used in <a href="#">ICAMS</a> . See <a href="#">CatalogRowOrder</a> for more details. If catalog is a vector, it will be converted to a 1-column matrix with rownames taken from the element names of the vector and with column name "Unknown".
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. Taken from <code>par("cex")</code> by default. Only implemented for SBS96Catalog, SBS192Catalog and DBS144Catalog.
grid	A logical value indicating whether to draw grid lines. Only implemented for SBS96Catalog, DBS78Catalog, IndelCatalog.
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, DBS78Catalog, IndelCatalog.
xlabels	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog, DBS78Catalog, IndelCatalog. If FALSE then plot x axis tick marks for SBS96Catalog; set <code>par(tck = 0)</code> to suppress.
ylabels	A logical value indicating whether to draw y axis labels. Only implemented for SBS96Catalog, DBS78Catalog, IndelCatalog.
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**

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file)
colnames(catSBS96) <- "sample"
PlotCatalog(catSBS96)
```

---

PlotCatalogToPdf

*Plot catalog to a PDF file*


---

**Description**

Plot catalog to a PDF file. The type of graph is based on 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,
  ylabels = NULL,
  ylim = NULL
)
```

**Arguments**

catalog	A catalog as defined in <a href="#">ICAMS</a> with attributes added. See <a href="#">as.catalog</a> for more details. catalog can also be a numeric matrix, numeric data.frame, or a vector denoting the mutation <b>counts</b> , but <b>must</b> be in the correct row order used in <a href="#">ICAMS</a> . See <a href="#">CatalogRowOrder</a> for more details. If catalog is a vector, it will be converted to a 1-column matrix with rownames taken from the element names of the vector and with column name "Unknown".
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, DBS78Catalog, IndelCatalog.
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, DBS78Catalog, IndelCatalog.
xlabels	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog, DBS78Catalog, IndelCatalog. If FALSE then plot x axis tick marks for SBS96Catalog; set par(tck = 0) to suppress.
ylabels	A logical value indicating whether to draw y axis labels. Only implemented for SBS96Catalog, DBS78Catalog, IndelCatalog.
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

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file)
colnames(catSBS96) <- "sample"
PlotCatalogToPdf(catSBS96, file = file.path(tempdir(), "test.pdf"))
```

---

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 <a href="#">AnnotateSBSVCF</a> . It <b>must</b> have transcript range information added.
expression.data	A <a href="#">data.table</a> which contains the expression values of genes. See <a href="#">GeneExpressionData</a> 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 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 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

```
file <- c(system.file("extdata/Strelka-SBS-vcf/",
                     "Strelka.SBS.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadAndSplitStrelkaSBSVCFs(file)
SBS.vcf <- list.of.vcfs$SBS.vcfs[[1]]
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  annotated.SBS.vcf <- AnnotateSBSVCF(SBS.vcf, ref.genome = "hg19",
                                     trans.ranges = trans.ranges.GRCh37)
  PlotTransBiasGeneExp(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>A")
}
```

---

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

<code>annotated.SBS.vcf</code>	An SBS VCF annotated by <a href="#">AnnotateSBSVCF</a> . It <b>must</b> have transcript range information added.
<code>file</code>	The name of output file.
<code>expression.data</code>	A <a href="#">data.table</a> which contains the expression values of genes. See <a href="#">GeneExpressionData</a> for more details.
<code>Ensembl.gene.ID.col</code>	Name of column which has the Ensembl gene ID information in <code>expression.data</code> .
<code>expression.value.col</code>	Name of column which has the gene expression values in <code>expression.data</code> .
<code>num.of.bins</code>	The number of bins that will be plotted on the graph.
<code>plot.type</code>	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.
<code>damaged.base</code>	One of NULL, "purine" or "pyrimidine". This function allocates approximately equal numbers of mutations from <code>damaged.base</code> into each of <code>num.of.bins</code> bin by expression level. E.g. if <code>damaged.base</code> 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 <code>damaged.base</code> 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 <code>damaged.base</code> 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/",
                     "Strelka.SBS.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadAndSplitStrelkaSBSVCFs(file)
SBS.vcf <- list.of.vcfs$SBS.vcfs[[1]]
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  annotated.SBS.vcf <- AnnotateSBSVCF(SBS.vcf, ref.genome = "hg19",
                                     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

**[Deprecated, use ReadAndSplitVCFs(variant.caller = "mutect") instead]** *Read and split Mutect VCF files*

---

## Description

**[Deprecated, use ReadAndSplitVCFs(variant.caller = "mutect") instead]** Read and split Mutect VCF files

## Usage

```

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

```

## Arguments

<code>files</code>	Character vector of file paths to the Mutect VCF files.
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Vector of column names or column indices in VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of VCFs specified in <code>files</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## 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**

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadAndSplitMutectVCFs(file)
```

---

ReadAndSplitStrelkaSBSVCFs

**[Deprecated, use `ReadAndSplitVCFs(variant.caller = "strelka")` instead]** *Read and split Strelka SBS VCF files*

---

**Description**

**[Deprecated, use `ReadAndSplitVCFs(variant.caller = "strelka")` instead]** 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**

<code>files</code>	Character vector of file paths to the Strelka SBS VCF files.
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

**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**

[StrelkaSBSCFFilesToCatalog](#)

**Examples**

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

---

ReadAndSplitVCFs	<i>Read and split VCF files</i>
------------------	---------------------------------

---

**Description**

Read and split VCF files

**Usage**

```
ReadAndSplitVCFs(
  files,
  variant.caller = "unknown",
  num.of.cores = 1,
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = "PASS",
  get.vaf.function = NULL,
  ...,
  max.vaf.diff = 0.02,
  suppress.discarded.variants.warnings = TRUE,
  always.merge.SBS = FALSE
)
```

**Arguments**

<code>files</code>	Character vector of file paths to the VCF files.
<code>variant.caller</code>	Name of the variant caller that produces the VCF, can be either "strelka", "mutect", "freebayes" or "unknown". This information is needed to calculate the VAFs (variant allele frequencies). If variant caller is "unknown" (default) and <code>get.vaf.function</code> is NULL, then VAF and read depth will be NAs. If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>names.of.VCFs</code>	Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . 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.

tumor.col.names	Optional. Only applicable to <b>Mutect</b> VCFs. Vector of column names or column indices in <b>Mutect</b> VCFs which contain the tumor sample information. The order of elements in tumor.col.names should match the order of <b>Mutect</b> VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the <b>Mutect</b> VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
filter.status	The character string in column FILTER of the VCF that indicates that a variant has passed all the variant caller's filters. Variants (lines in the VCF) for which the value in column FILTER does not equal filter.status are silently excluded from the output. If NULL, all variants are retained. In almost all cases, the default value of "PASS" is what the user would want.
get.vaf.function	Optional. Only applicable when variant.caller is " <b>unknown</b> ". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See <a href="#">GetMutectVAF</a> as an example. If NULL(default) and variant.caller is "unknown", then VAF and read depth will be NAs.
...	Optional arguments to get.vaf.function.
max.vaf.diff	<b>Not</b> applicable if variant.caller = "mutect". The maximum difference of VAF, default value is 0.02. If the absolute difference of VAFs for adjacent SBSs is bigger than max.vaf.diff, then these adjacent SBSs are likely to be "merely" asynchronous single base mutations, opposed to a simultaneous doublet mutation or variants involving more than two consecutive bases.
suppress.discarded.variants.warnings	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.
always.merge.SBS	If TRUE merge adjacent SBSs as DBSs regardless of VAFs and regardless of the value of max.vaf.diff and regardless of the value of get.vaf.function. It is an error to set this to TRUE when variant.caller = "mutect".

## 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

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadAndSplitVCFs(file, variant.caller = "mutect")
```

ReadCatalog

*Read catalog***Description**

Read a catalog in standardized format from path.

**Usage**

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

**Arguments**

- |               |  |
|---------------|--|
| file          | Path to a catalog on disk in a standardized format. The recognized formats are: <ul style="list-style-type: none"> <li>• ICAMS formatted SBS96, SBS192, SBS1536, DBS78, DBS136, DBS144, ID (see <a href="#">CatalogRowOrder</a>).</li> <li>• SigProfiler-formatted SBS96, DBS78 and ID83 catalogs; see <a href="https://github.com/AlexandrovLab/SigProfilerExtractor">https://github.com/AlexandrovLab/SigProfilerExtractor</a>.</li> <li>• COSMIC-formatted SBS96, SBS192 (a.k.a. TSB192), DBS78, ID83 catalogs; see <a href="https://cancer.sanger.ac.uk/signatures/">https://cancer.sanger.ac.uk/signatures/</a>.</li> </ul> |
| ref.genome    | A ref.genome argument as described in <a href="#">ICAMS</a> .  |
| region        | region A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .   |
| catalog.type  | One of "counts", "density", "counts.signature", "density.signature".   |
| strict        | Ignored and deprecated.  |
| stop.on.error | If TRUE, call stop on error; otherwise return a 1-column matrix of NA's with the attribute "error" containing error information. The number of rows may not be the correct number for the expected catalog type.   |

**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 insertions and deletions) 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**

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file)
```

---

ReadStrelkaIDVCFs	<b>[Deprecated, use ReadAndSplitVCFs(variant.caller = "strelka") instead]</b> <i>Read Strelka ID (small insertions and deletions) VCF files</i>
-------------------	---

---

**Description**

**[Deprecated, use ReadAndSplitVCFs(variant.caller = "strelka") instead]** Read Strelka ID (small insertions and deletions) 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 insertions and deletions) 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**

```
file <- c(system.file("extdata/Strelka-ID-vcf",
                    "Strelka.ID.GRCh37.s1.vcf",
                    package = "ICAMS"))
list.of.vcfs <- ReadStrelkaIDVCFs(file)
```



ReadVCFs

*Read VCF files***Description**

Read VCF files

**Usage**

```
ReadVCFs(
  files,
  variant.caller = "unknown",
  num.of.cores = 1,
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = "PASS",
  get.vaf.function = NULL,
  ...
)
```

**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", "freebayes" or "unknown". This information is needed to calculate the VAFs (variant allele frequencies). If variant caller is "unknown"(default) and get.vaf.function is NULL, then VAF and read depth will be NAs. If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.   |
| num.of.cores    | The number of cores to use. Not available on Windows unless num.of.cores = 1.  |
| 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.  |
| tumor.col.names | Optional. Only applicable to <b>Mutect</b> VCFs. Vector of column names or column indices in <b>Mutect</b> VCFs which contain the tumor sample information. The order of elements in tumor.col.names should match the order of <b>Mutect</b> VCFs specified in files. If tumor.col.names is equal to NA(default), this function will use the 10th column in all the <b>Mutect</b> VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details. |
| filter.status   | The character string in column FILTER of the VCF that indicates that a variant has passed all the variant caller's filters. Variants (lines in the VCF) for which the value in column FILTER does not equal filter.status are silently excluded from the output. If NULL, all variants are retained. In almost all cases, the default value of "PASS" is what the user would want.   |

`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.

... Optional arguments to `get.vaf.function`.

### Value

A list of data frames storing data lines of the VCF files with two additional columns added which contain the VAF(variant allele frequency) and read depth information.

### Examples

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadVCFs(file, variant.caller = "mutect")
```

---

revc

*Reverse complement every string in string.vec*

---

### Description

Based on [reverseComplement](#). Handles IUPAC ambiguity codes but not "u" (uracil). (see <[https://en.wikipedia.org/wiki/Nucleic\\_acid\\_notation](https://en.wikipedia.org/wiki/Nucleic_acid_notation)>).

### 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)
```

---

SimpleReadVCF	<i>Read a VCF file into a data frame with minimal processing.</i>
---------------	---

---

**Description**

Read a VCF file into a data frame with minimal processing.

**Usage**

```
SimpleReadVCF(file)
```

**Arguments**

file	The name/path of the VCF file, or a complete URL.
------	---

**Details**

Header lines beginning "##" are removed, and column "#CHROM" is renamed to "CHROM". Other column names are unchanged. Columns "#CHROM", "POS", "REF", and "ALT" must be in the input.

**Value**

A data frame storing mutation records of a VCF file.

**Examples**

```
file <- c(system.file("extdata/Strelka-SBS-vcf",
                      "Strelka.SBS.GRCh37.s1.vcf",
                      package = "ICAMS"))
df <- SimpleReadVCF(file)
```

---

SplitListOfVCFs	<i>Split each VCF into SBS, DBS, and ID VCFs (plus VCF-like data frame with left-over rows)</i>
-----------------	---

---

**Description**

Split each VCF into SBS, DBS, and ID VCFs (plus VCF-like data frame with left-over rows)

**Usage**

```
SplitListOfVCFs(
  list.of.vcfs,
  variant.caller,
  max.vaf.diff = 0.02,
  num.of.cores = 1,
  suppress.discarded.variants.warnings = TRUE,
  always.merge.SBS = FALSE
)
```

**Arguments**

<code>list.of.vcfs</code>	List of VCFs as in-memory data frames. The VCFs should have VAF and <code>read.depth</code> information added. See <code>ReadVCFs</code> for more details.
<code>variant.caller</code>	Name of the variant caller that produces the VCF, can be either "strelka", "mutect", "freebayes" or "unknown". If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.
<code>max.vaf.diff</code>	The maximum difference of VAF, default value is 0.02. If the absolute difference of VAFs for adjacent SBSs is bigger than <code>max.vaf.diff</code> , then these adjacent SBSs are likely to be "merely" asynchronous single base mutations, opposed to a simultaneous doublet mutation or variants involving more than two consecutive bases.
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.
<code>always.merge.SBS</code>	If TRUE merge adjacent SBSs as DBSs regardless of VAFs and regardless of the value of <code>max.vaf.diff</code> and regardless of the value of <code>get.vaf.function</code> . It is an error to set this to TRUE when <code>variant.caller = "mutect"</code> .

**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.

**Examples**

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.vcfs <- ReadVCFs(file, variant.caller = "mutect")
split.vcfs <- SplitListOfVCFs(list.of.vcfs, variant.caller = "mutect")
```

---

StrelkaIDVCFFilesToCatalog

**[Deprecated, use `VCFsToCatalogs(variant.caller = "strelka")` instead]** Create ID (small insertions and deletions) catalog from Strelka ID VCF files

---

**Description**

**[Deprecated, use `VCFsToCatalogs(variant.caller = "strelka")` instead]** Create ID (small insertions and deletions) 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**

<code>files</code>	Character vector of file paths to the Strelka ID VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

**Details**

This function calls [VCFsToIDCatalogs](#)

**Value**

A **list** of elements:

- `catalog`: The ID (small insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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

```
file <- c(system.file("extdata/Strelka-ID-vcf",
                     "Strelka.ID.GRCh37.s1.vcf",
                     package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catID <- StrelkaIDVCFFilesToCatalog(file, ref.genome = "hg19",
                                     region = "genome")}
```

---

StrelkaIDVCFFilesToCatalogAndPlotToPdf

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "strelka")` instead]** Create ID (small insertions and deletions) catalog from Strelka ID VCF files and plot them to PDF

---

## Description

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "strelka")` instead]** Create ID (small insertions and deletions) catalog from the Strelka ID VCFs specified by files and plot them to PDF

## Usage

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

**Arguments**

<code>files</code>	Character vector of file paths to the Strelka ID VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>output.file</code>	Optional. The base name of the PDF file to be produced; the file is ending in <code>catID.pdf</code> .
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

**Details**

This function calls [StrelkaIDVCFFilesToCatalog](#) and [PlotCatalogToPdf](#)

**Value**

A **list** of elements:

- `catalog`: The ID (small insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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**

```
file <- c(system.file("extdata/Strelka-ID-vcf",
                     "Strelka.ID.GRCh37.s1.vcf",
                     package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catID <-
    StrelkaIDVCFFilesToCatalogAndPlotToPdf(file, ref.genome = "hg19",
                                           region = "genome",
                                           output.file =
                                           file.path(tempdir(), "StrelkaID"))}
```

---

StrelkaIDVCFFilesToZipFile

**[Deprecated, use `VCFsToZipFile(variant.caller = "strelka")` instead]** Create a zip file which contains ID (small insertions and deletions) catalog and plot PDF from Strelka ID VCF files

---

**Description**

**[Deprecated, use `VCFsToZipFile(variant.caller = "strelka")` instead]** Create ID (small insertions and deletions) 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**

<code>dir</code>	Pathname of the directory which contains <b>only</b> the Strelka ID VCF files. Each Strelka ID VCF <b>must</b> have a file extension ".vcf" (case insensitive) and share the <b>same</b> <code>ref.genome</code> and <code>region</code> .
<code>zipfile</code>	Pathname of the zip file to be created.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .



<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCFs listed in <code>dir</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>dir</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>base.filename</code>	Optional. The base name of the CSV and PDF file to be produced; the file is ending in <code>catID.csv</code> and <code>catID.pdf</code> respectively.
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## Details

This function calls [StrelkaIDVCFFilesToCatalog](#), [PlotCatalogToPdf](#), [WriteCatalog](#) and `zip::zipr`.

## Value

A **list** of elements:

- `catalog`: The ID (small insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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

```
dir <- c(system.file("extdata/Strelka-ID-vcf",
                    package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <-
    StrelkaIDVCFFilesToZipFile(dir,
                               zipfile = file.path(tempdir(), "test.zip"),
                               ref.genome = "hg19",
                               region = "genome",
                               base.filename = "Strelka-ID")
  unlink(file.path(tempdir(), "test.zip"))}
```

---

StrelkaSBSVCFFilesToCatalog

**[Deprecated, use `VCFsToCatalogs(variant.caller = "strelka")` instead]** Create SBS and DBS catalogs from Strelka SBS VCF files

---

## Description

**[Deprecated, use `VCFsToCatalogs(variant.caller = "strelka")` instead]** 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

<code>files</code>	Character vector of file paths to the Strelka SBS VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .



---

StrelkaSBSVCFFilesToCatalogAndPlotToPdf

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "strelka")` instead]** Create SBS and DBS catalogs from Strelka SBS VCF files and plot them to PDF

---

## Description

**[Deprecated, use `VCFsToCatalogsAndPlotToPdf(variant.caller = "strelka")` instead]** 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

<code>files</code>	Character vector of file paths to the Strelka SBS VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li><code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li><code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li><code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>output.file</code>	Optional. The base name of the PDF files to be produced; multiple files will be generated, each ending in <code>x.pdf</code> , where <code>x</code> indicates the type of catalog plotted in the file.



---

StrelkaSBSVCFFilesToZipFile

**[Deprecated, use VCFsToZipFile(variant.caller = "strelka") instead]** Create a zip file which contains catalogs and plot PDFs from Strelka SBS VCF files

---

## Description

**[Deprecated, use VCFsToZipFile(variant.caller = "strelka") instead]** 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

<code>dir</code>	Pathname of the directory which contains <b>only</b> the Strelka SBS VCF files. Each Strelka SBS VCF <b>must</b> have a file extension ".vcf" (case insensitive) and share the <b>same</b> <code>ref.genome</code> and region.
<code>zipfile</code>	Pathname of the zip file to be created.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCFs listed in <code>dir</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>dir</code> 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.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.

## Details

This function calls [StrelkaSBSVCFFilesToCatalog](#), [PlotCatalogToPdf](#), [WriteCatalog](#) and `zip::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.

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

```
dir <- c(system.file("extdata/Strelka-SBS-vcf",
                    package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <-
    StrelkaSBSVCFFilesToZipFile(dir,
                                zipfile = file.path(tempdir(), "test.zip"),
                                ref.genome = "hg19",
                                trans.ranges = trans.ranges.GRCh37,
                                region = "genome",
                                base.filename = "Strelka-SBS")
  unlink(file.path(tempdir(), "test.zip"))
}
```





---

TranscriptRanges	<i>Transcript ranges data</i>
------------------	-------------------------------

---

## 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.

## 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/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_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](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
#      1      65419      71585      + ENSG00000186092    OR4F5
#      1     367640     368634      + ENSG00000235249    OR4F29
#      1     621059     622053      - ENSG00000284662    OR4F16
#      1     859308     879961      + ENSG00000187634    SAMD11
#      1     879583     894689      - ENSG00000188976    NOC2L
#      ...           ...           ...           ...           ...           ...
```

---

TransformCatalog	<i>Transform between counts and density spectrum catalogs and counts and density signature catalogs</i>
------------------	---

---

## 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
)
```

## Arguments

catalog	An SBS or DBS catalog as described in <a href="#">ICAMS</a> ; must <b>not</b> be an ID (small insertions and deletions) catalog.
target.ref.genome	A ref.genome argument as described in <a href="#">ICAMS</a> . If NULL, then defaults to the ref.genome attribute of catalog.
target.region	A region argument; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> . 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 <a href="#">as.catalog</a> . 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 strand-agnostic single nucleotide substitutions in trinucleotide – i.e. 3-mer – context, one count each for ACA, ACC, ACG, ... TTT). See <a href="#">all.abundance</a> . 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.

## Details

Only the following transformations are legal:

1. 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](#).

## 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

```
file <- system.file("extdata",
  "strelka.regress.cat.sbs.96.csv",
  package = "ICAMS")
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catSBS96.counts <- ReadCatalog(file, ref.genome = "hg19",
    region = "genome",
    catalog.type = "counts")
  catSBS96.density <- TransformCatalog(catSBS96.counts,
    target.ref.genome = "hg19",
    target.region = "genome",
    target.catalog.type = "density")}
```

---

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",
  num.of.cores = 1,
  trans.ranges = NULL,
  region = "unknown",
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = "PASS",
  get.vaf.function = NULL,
  ...,
  max.vaf.diff = 0.02,
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

## Arguments

<code>files</code>	Character vector of file paths to the VCF files.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>variant.caller</code>	Name of the variant caller that produces the VCF, can be either "strelka", "mutect", "freebayes" or "unknown". This information is needed to calculate the VAFs (variant allele frequencies). If variant caller is "unknown" (default) and <code>get.vaf.function</code> is NULL, then VAF and read depth will be NAs. If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .

<code>trans.ranges</code>	<p>Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object</p> <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> <p>then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code>. Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.</p>
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Only applicable to <b>Mutect</b> VCFs. Vector of column names or column indices in <b>Mutect</b> VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of <b>Mutect</b> VCFs specified in <code>files</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the <b>Mutect</b> VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>filter.status</code>	The character string in column <code>FILTER</code> of the VCF that indicates that a variant has passed all the variant caller's filters. Variants (lines in the VCF) for which the value in column <code>FILTER</code> does not equal <code>filter.status</code> are silently excluded from the output. If <code>NULL</code> , all variants are retained. In almost all cases, the default value of "PASS" is what the user would want.
<code>get.vaf.function</code>	Optional. Only applicable when <code>variant.caller</code> is "unknown". Function to calculate VAF (variant allele frequency) and read depth information from original VCF. See <a href="#">GetMutectVAF</a> as an example. If <code>NULL</code> (default) and <code>variant.caller</code> is "unknown", then VAF and read depth will be NAs.
<code>...</code>	Optional arguments to <code>get.vaf.function</code> .
<code>max.vaf.diff</code>	<b>Not</b> applicable if <code>variant.caller = "mutect"</code> . The maximum difference of VAF, default value is 0.02. If the absolute difference of VAFs for adjacent SBSs is bigger than <code>max.vaf.diff</code> , then these adjacent SBSs are likely to be "merely" asynchronous single base mutations, opposed to a simultaneous doublet mutation or variants involving more than two consecutive bases.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## 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 insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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**

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <- VCFsToCatalogs(file, ref.genome = "hg19",
                             variant.caller = "mutect", region = "genome")}
```

---

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",
  num.of.cores = 1,
  trans.ranges = NULL,
  region = "unknown",
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = "PASS",
  get.vaf.function = NULL,
  ...,
  max.vaf.diff = 0.02,
  base.filename = "",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

## Arguments

<code>files</code>	Character vector of file paths to the VCF files.
<code>output.dir</code>	The directory where the PDF files will be saved.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>variant.caller</code>	Name of the variant caller that produces the VCF, can be either "strelka", "mutect", "freebayes" or "unknown". This information is needed to calculate the VAFs (variant allele frequencies). If variant caller is "unknown" (default) and <code>get.vaf.function</code> is NULL, then VAF and read depth will be NAs. If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.

<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>names.of.VCFs</code>	Optional. Character vector of names of the VCF files. The order of names in <code>names.of.VCFs</code> should match the order of VCF file paths in <code>files</code> . If <code>NULL</code> (default), this function will remove all of the path up to and including the last path separator (if any) in <code>files</code> and file paths without extensions (and the leading dot) will be used as the names of the VCF files.
<code>tumor.col.names</code>	Optional. Only applicable to <b>Mutect</b> VCFs. Vector of column names or column indices in <b>Mutect</b> VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of <b>Mutect</b> VCFs specified in <code>files</code> . If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the <b>Mutect</b> VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>filter.status</code>	The character string in column <code>FILTER</code> of the VCF that indicates that a variant has passed all the variant caller's filters. Variants (lines in the VCF) for which the value in column <code>FILTER</code> does not equal <code>filter.status</code> are silently excluded from the output. If <code>NULL</code> , all variants are retained. In almost all cases, the default value of "PASS" is what the user would want.
<code>get.vaf.function</code>	Optional. Only applicable when <code>variant.caller</code> is " <b>unknown</b> ". Function to calculate VAF (variant allele frequency) and read depth information from original VCF. See <a href="#">GetMutectVAF</a> as an example. If <code>NULL</code> (default) and <code>variant.caller</code> is "unknown", then VAF and read depth will be <code>NA</code> s.
<code>...</code>	Optional arguments to <code>get.vaf.function</code> .
<code>max.vaf.diff</code>	<b>Not</b> applicable if <code>variant.caller = "mutect"</code> . The maximum difference of VAF, default value is 0.02. If the absolute difference of VAFs for adjacent SBSs is bigger than <code>max.vaf.diff</code> , then these adjacent SBSs are likely to be "merely" asynchronous single base mutations, opposed to a simultaneous doublet mutation or variants involving more than two consecutive bases.
<code>base.filename</code>	Optional. The base name of the PDF files to be produced; multiple files will be generated, each ending in <code>x.pdf</code> , where <code>x</code> indicates the type of catalog plotted in the file.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## 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).





---

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 than DBSs.

## Usage

```
VCFsToDBSCatalogs(
  list.of.DBS.vcfs,
  ref.genome,
  num.of.cores = 1,
  trans.ranges = NULL,
  region = "unknown",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

## Arguments

<code>list.of.DBS.vcfs</code>	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.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.
<code>suppress.discarded.variants.warnings</code>	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.
- 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

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.DBS.vcfs <- ReadAndSplitMutectVCFs(file)$DBS
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs.DBS <- VCFsToDBSCatalogs(list.of.DBS.vcfs, ref.genome = "hg19",
                                    trans.ranges = trans.ranges.GRCh37,
                                    region = "genome")}
```

---

VCFsToIDCatalogs

---

*Create ID (small insertions and deletions) catalog from ID VCFs*


---

## Description

Create ID (small insertions and deletions) catalog from ID VCFs

## Usage

```
VCFsToIDCatalogs(
  list.of.vcfs,
  ref.genome,
  num.of.cores = 1,
  region = "unknown",
  flag.mismatches = 0,
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

**Arguments**

<code>list.of.vcfs</code>	List of in-memory ID VCFs. The list names will be the sample ids in the output catalog.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>region</code>	A character string acting as a region identifier, one of "genome", "exome".
<code>flag.mismatches</code>	Deprecated. If there are ID variants whose REF do not match the extracted sequence from <code>ref.genome</code> , the function will automatically discard these variants and an element <code>discarded.variants</code> will appear in the return value. See <a href="#">AnnotateIDVCF</a> for more details.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is FALSE.
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is TRUE.

**Value**

A **list** of elements:

- `catalog`: The ID (small insertions and deletions) 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 insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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**

```
file <- c(system.file("extdata/Strelka-ID-vcf/",
                     "Strelka.ID.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.ID.vcfs <- ReadStrelkaIDVCFs(file)
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5",
                     quietly = TRUE)) {
  catID <- VCFsToIDCatalogs(list.of.ID.vcfs, ref.genome = "hg19",
                           region = "genome")}
```

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,
  num.of.cores = 1,
  trans.ranges = NULL,
  region = "unknown",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

**Arguments**

<code>list.of.SBS.vcfs</code>	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.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in <a href="#">ICAMS</a> .
<code>num.of.cores</code>	The number of cores to use. Not available on Windows unless <code>num.of.cores = 1</code> .
<code>trans.ranges</code>	Optional. If <code>ref.genome</code> specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. <code>BSgenome.Hsapiens.1000genomes.hs37d5</code></li> <li>2. <code>BSgenome.Hsapiens.UCSC.hg38</code></li> <li>3. <code>BSgenome.Mmusculus.UCSC.mm10</code></li> </ol> then the function will infer <code>trans.ranges</code> automatically. Otherwise, user will need to provide the necessary <code>trans.ranges</code> . Please refer to <a href="#">TranscriptRanges</a> for more details. If <code>is.null(trans.ranges)</code> do not add transcript range information.
<code>region</code>	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .

`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.
- `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

```
file <- c(system.file("extdata/Mutect-vcf",
                     "Mutect.GRCh37.s1.vcf",
                     package = "ICAMS"))
list.of.SBS.vcfs <- ReadAndSplitMutectVCFs(file)$SBS
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs.SBS <- VCFsToSBSCatalogs(list.of.SBS.vcfs, ref.genome = "hg19",
                                   trans.ranges = trans.ranges.GRCh37,
                                   region = "genome")}
```

---

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,
  files,
  zipfile,
  ref.genome,
  variant.caller = "unknown",
  num.of.cores = 1,
  trans.ranges = NULL,
  region = "unknown",
  names.of.VCFs = NULL,
  tumor.col.names = NA,
  filter.status = "PASS",
  get.vaf.function = NULL,
  ...,
  max.vaf.diff = 0.02,
  base.filename = "",
  return.annotated.vcfs = FALSE,
  suppress.discarded.variants.warnings = TRUE
)
```

**Arguments**

dir	Pathname of the directory which contains VCFs that come from the <b>same</b> variant caller. Each VCF <b>must</b> have a file extension ".vcf" (case insensitive) and share the <b>same</b> ref.genome and region.
files	Character vector of file paths to the VCF files. Only <b>one</b> of argument dir or files need to be specified.
zipfile	Pathname of the zip file to be created.
ref.genome	A ref.genome argument as described in <a href="#">ICAMS</a> .
variant.caller	Name of the variant caller that produces the VCF, can be either "strelka", "mutect", "freebayes" or "unknown". This information is needed to calculate the VAFs (variant allele frequencies). If variant caller is "unknown"(default) and get.vaf.function is NULL, then VAF and read depth will be NAs. If variant caller is "mutect", do <b>not</b> merge SBSs into DBS.
num.of.cores	The number of cores to use. Not available on Windows unless num.of.cores = 1.
trans.ranges	Optional. If ref.genome specifies one of the <a href="#">BSgenome</a> object <ol style="list-style-type: none"> <li>1. BSgenome.Hsapiens.1000genomes.hs37d5</li> <li>2. BSgenome.Hsapiens.UCSC.hg38</li> <li>3. BSgenome.Mmusculus.UCSC.mm10</li> </ol> then the function will infer trans.ranges automatically. Otherwise, user will need to provide the necessary trans.ranges. Please refer to <a href="#">TranscriptRanges</a> for more details. If is.null(trans.ranges) do not add transcript range information.
region	A character string designating a genomic region; see <a href="#">as.catalog</a> and <a href="#">ICAMS</a> .
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.

<code>tumor.col.names</code>	Optional. Only applicable to <b>Mutect</b> VCFs. Vector of column names or column indices in <b>Mutect</b> VCFs which contain the tumor sample information. The order of elements in <code>tumor.col.names</code> should match the order of <b>Mutect</b> VCFs specified in files. If <code>tumor.col.names</code> is equal to <code>NA</code> (default), this function will use the 10th column in all the <b>Mutect</b> VCFs to calculate VAFs. See <a href="#">GetMutectVAF</a> for more details.
<code>filter.status</code>	The character string in column <code>FILTER</code> of the VCF that indicates that a variant has passed all the variant caller's filters. Variants (lines in the VCF) for which the value in column <code>FILTER</code> does not equal <code>filter.status</code> are silently excluded from the output. If <code>NULL</code> , all variants are retained. In almost all cases, the default value of "PASS" is what the user would want.
<code>get.vaf.function</code>	Optional. Only applicable when <code>variant.caller</code> is "unknown". Function to calculate VAF(variant allele frequency) and read depth information from original VCF. See <a href="#">GetMutectVAF</a> as an example. If <code>NULL</code> (default) and <code>variant.caller</code> is "unknown", then VAF and read depth will be NAs.
<code>...</code>	Optional arguments to <code>get.vaf.function</code> .
<code>max.vaf.diff</code>	<b>Not</b> applicable if <code>variant.caller = "mutect"</code> . The maximum difference of VAF, default value is 0.02. If the absolute difference of VAFs for adjacent SBSs is bigger than <code>max.vaf.diff</code> , then these adjacent SBSs are likely to be "merely" asynchronous single base mutations, opposed to a simultaneous doublet mutation or variants involving more than two consecutive bases.
<code>base.filename</code>	Optional. The base name of the CSV and PDF files to be produced; multiple files will be generated, each ending in <code>x.csv</code> or <code>x.pdf</code> , where <code>x</code> indicates the type of catalog.
<code>return.annotated.vcfs</code>	Logical. Whether to return the annotated VCFs with additional columns showing mutation class for each variant. Default is <code>FALSE</code> .
<code>suppress.discarded.variants.warnings</code>	Logical. Whether to suppress warning messages showing information about the discarded variants. Default is <code>TRUE</code> .

## Details

This function calls [VCFsToCatalogs](#), [PlotCatalogToPdf](#), [WriteCatalog](#) and `zip::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 insertions and deletions) 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\\_2021\\_09\\_03.xlsx](https://github.com/steverozen/ICAMS/raw/master/data-raw/PCAWG7_indel_classification_2021_09_03.xlsx) for additional information on ID (small insertions and deletions) 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 insertions and deletions) 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

```
dir <- c(system.file("extdata/Mutect-vcf",
  package = "ICAMS"))
if (requireNamespace("BSgenome.Hsapiens.1000genomes.hs37d5", quietly = TRUE)) {
  catalogs <-
    VCFsToZipFile(dir,
      zipfile = file.path(tempdir(), "test.zip"),
      ref.genome = "hg19",
      variant.caller = "mutect",
      region = "genome",
      base.filename = "Mutect")
  unlink(file.path(tempdir(), "test.zip"))
}
```

---

WriteCatalog	<i>Write a catalog</i>
--------------	------------------------

---

**Description**

Write a catalog to a file.

**Usage**

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

**Arguments**

catalog	A catalog as defined in <a href="#">ICAMS</a> ; see also <a href="#">as.catalog</a> .
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 insertions and deletions) 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**

```
file <- system.file("extdata",  
                    "strelka.regress.cat.sbs.96.csv",  
                    package = "ICAMS")  
catSBS96 <- ReadCatalog(file)  
WriteCatalog(catSBS96, file = file.path(tempdir(), "catSBS96.csv"))
```

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