

Package ‘ICAMS’

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Type Package

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

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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>. ``ICAMS" stands for In-depth Characterization and Analysis of Mutational Signatures. ICAMS has functions to read in variant call files (VCFs) and to collate the corresponding catalogs of mutational spectra and to analyze and plot catalogs of mutational spectra and signatures. Handles both ``counts-based" and ``density-based" catalogs of mutational spectra or signatures.

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BSgenome.Hsapiens.1000genomes.hs37d5,
BSgenome.Hsapiens.UCSC.hg38,
BSgenome.Mmusculus.UCSC.mm10,
data.table,
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graphics,
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IRanges,
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R topics documented:

all.abundance	2
as.catalog	3
CatalogRowOrder	4
CollapseCatalog	4
FindDelMH	5
GetVAF	7
ICAMS	8
MutectVCFFilesToCatalog	11
MutectVCFFilesToCatalogAndPlotToPdf	12
PlotCatalog	13
PlotCatalogToPdf	14
ReadAndSplitMutectVCFs	15
ReadAndSplitStrelkaSBSVCFs	16
ReadCatalog	16
ReadStrelkaIDVCFs	17
revc	18
StrelkaIDVCFFilesToCatalog	19
StrelkaIDVCFFilesToCatalogAndPlotToPdf	19
StrelkaSBSVCFFilesToCatalog	20
StrelkaSBSVCFFilesToCatalogAndPlotToPdf	21
TranscriptRanges	22
TransformCatalog	23
VCFsToDBSCatalogs	25
VCFsToIDCatalogs	26
VCFsToSBSCatalogs	26
WriteCatalog	27
Index	29

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.
```

as.catalog	Create a catalog from a numeric matrix or numeric data.frame.
------------	---

Description

Create a catalog from a numeric matrix or numeric data.frame.

Usage

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

Arguments

object	A numeric matrix or numeric data.frame. This object must have rownames to denote the mutation types. See CatalogRowOrder for more details.
ref.genome	A ref.genome argument as described in ICAMS .
region	A character string designating a region, one of genome, transcript, exome, unknown; see ICAMS .
catalog.type	One of "counts", "density", "counts.signature", "density.signature".
abundance	If NULL, then inferred if ref.genome is one of the reference genomes known to ICAMS and region is not unknown. See ICAMS . The argument abundance should contain the counts of different source sequences for mutations in the same format as the numeric vectors in all.abundance .

Value

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

Examples

```
# Create an SBS96 catalog of human GRCh37 from genome region with all
# mutation counts equal to 1.
object <- matrix(1, nrow = 96, ncol = 1,
  dimnames = list(catalog.row.order$SBS96))
catSBS96 <- as.catalog(object, ref.genome = "hg19", region = "genome")
```

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.

Note

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

Examples

```
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, ref.genome = "hg19", region = "transcript")
catSBS96 <- Collapse192CatalogTo96(catSBS192)
```

FindDelMH

Return the length of microhomology at a deletion.

Description

Return the length of microhomology at a deletion.

Usage

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

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, cat various messages.

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
                        ****  ****

```

A deletion in a *repeat* can also be represented in several different ways. A deletion in a repeat is abstractly equivalent to 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 this case with a -1 return; it does not figure out the repeat extent.

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).

Value

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

Examples

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

GetVAF

Extract the VAFs (variant allele frequencies) from a VCF file.

Description

Extract the VAFs (variant allele frequencies) from a VCF file.

Usage

```
GetStrelkaVAF(vcf)
```

```
GetMutectVAF(vcf)
```

Arguments

`vcf` Said VCF as a `data.frame`.

Value

A vector of VAFs, one for each row of `vcf`.

Examples

```
file <- c(system.file("extdata",
                      "Strelka.SBS.GRCh37.vcf",
                      package = "ICAMS"))
MakeDataFrameFromStrelkaSBSVCF <-
  getFromNamespace("MakeDataFrameFromStrelkaSBSVCF", "ICAMS")
df <- MakeDataFrameFromStrelkaSBSVCF(file)
vaf <- GetStrelkaVAF(df)
```

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>. "ICAMS" stands for In-depth Characterization and Analysis of Mutational Signatures. ICAMS has functions to read in variant call files (VCFs) and to collate the corresponding catalogs of mutational spectra and to analyze and plot catalogs of mutational spectra and signatures. Handles both "counts-based" and "density-based" catalogs of mutational spectra or signatures.

Details

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

Catalogs

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

Catalogs are R S3 objects of class `matrix` and one of several additional classes that specify the types of the mutations represented in the catalog (e.g. `SBS96`, `ID`, etc, ...). The possible additional classes are one of `SBS96Catalog`, `SBS192Catalog`, `SBS1536Catalog`, `DBS78Catalog`, `DBS144Catalog`, `DBS136Catalog`, `IndelCatalog`. [as.catalog](#) is the main constructor.

Conceptually, a catalog has one of the following types, which are indicated in 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 below under [TransformCatalog](#) for more information. Abundances logically depend on the species in question and on the part of the genome being analyzed.

In ICAMS functions these can sometimes be inferred from catalog class attribute and function arguments `region`, `ref.genome`, and `catalog.type`. Otherwise they can be provided as an abundance argument. See [all.abundance](#) for examples.

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

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

Creating catalogs from variant call files (VCF files)

1. [StrelkaSBSVCFFilesToCatalog](#) creates 3 SBS catalogs (96, 192, 1536) and 3 DBS catalogs (78, 136, 144) from the Strelka SBS VCFs.
2. [StrelkaIDVCFFilesToCatalog](#) creates ID (indel) catalog from the Strelka ID VCFs.
3. [MutectVCFFilesToCatalog](#) creates 3 SBS catalogs (96, 192, 1536), 3 DBS catalogs (78, 136, 144) and ID (indel) catalog from the Mutect VCFs.

Plotting catalogs

The [PlotCatalog](#) functions plot mutational spectra for **one** sample or plot **one** mutational signature.

The [PlotCatalogToPdf](#) functions plot catalogs of mutational spectra or of mutational signatures to a PDF file.

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

1. [StrelkaSBSVCFFilesToCatalogAndPlotToPdf](#) creates all type of SBS and DBS catalogs from Strelka SBS VCFs and plots the catalogs.
2. [StrelkaIDVCFFilesToCatalog](#) creates an ID (indel) catalog from Strelka ID VCFs and plot it.
3. [MutectVCFFilesToCatalog](#) creates all types of SBS, DBS, and ID catalogs from Mutect VCFs and plots the catalogs.

The `ref.genome` (reference genome) argument

Many functions take the argument `ref.genome`.

In order to create a mutational spectrum catalog, ICAMS needs to know the sequence context of the mutations in the VCF file. For this, ICAMS needs the reference genome sequence that matches the VCF file. The `ref.genome` argument provides this.

`ref.genome` can be either

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"` are shorthand for [BSgenome.Hsapiens.UCSC.hg38](#), the strings `"hg19"` or `"GRCh37"` are shorthand for [BSgenome.Hsapiens.1000genomes.hs37d5](#), and the strings `"mm10"` or `"GRCm38"` are shorthand for [BSgenome.Mmusculus.UCSC.mm10](#).

The Bioconductor [BSgenome](#) package, two human genomes and one mouse genome from [BSgenome](#) are "imported" by ICAMS and therefore should be installed when ICAMS is installed. The three genomes that are installed as dependencies are:

- [BSgenome.Hsapiens.1000genomes.hs37d5](#)
- [BSgenome.Hsapiens.UCSC.hg38](#)

- `BSgenome.Mmusculus.UCSC.mm10`

Any other needed reference genomes must be installed separately by the user. Use `available.genomes()` to get the list of available genomes. Further instructions are at <https://bioconductor.org/packages/release/bioc/html/BSgenome.html>.

Use of ICAMS with other reference genomes is restricted to `catalog.type` of counts or `counts.signature` unless the user also creates the necessary abundance vectors. See [all.abundance](#).

Writing catalogs to files

The `WriteCatalog` functions write a catalog to a file.

Reading catalogs

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

Transforming catalogs

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

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

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

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

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

Collapsing catalogs

The `CollapseCatalog` functions

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

Data

1. [CatalogRowOrder](#) Standard order of rownames in a catalog. The rownames of encode the type of each mutation. The rownames denote the mutation types. 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.

MutectVCFFilesToCatalog

Create SBS, DBS and Indel catalogs from Mutect VCF files

Description

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

Usage

```
MutectVCFFilesToCatalog(files, ref.genome, trans.ranges = NULL,
  region = "unknown")
```

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 ICAMS .
<code>trans.ranges</code>	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .

Details

This function calls [VCFsToSBSCatalogs](#), [VCFsToDBSCatalogs](#) and [VCFsToIDCatalogs](#)

Value

A list of 3 SBS catalogs (one each for 96, 192, and 1536), 3 DBS catalogs (one each for 78, 136, and 144) and ID catalog. If `trans.ranges = NULL`, 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.

Examples

```
file <- c(system.file("extdata",
  "Mutect.GRCh37.vcf",
  package = "ICAMS"))
catalogs <- MutectVCFFilesToCatalog(file, ref.genome = "hg19",
  trans.ranges = trans.ranges.GRCh37,
  region = "genome")
```

MutectVCFFilesToCatalogAndPlotToPdf

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

Description

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

Usage

```
MutectVCFFilesToCatalogAndPlotToPdf(files, ref.genome,
  trans.ranges = NULL, region = "unknown", output.file)
```

Arguments

files	Character vector of file paths to the Mutect VCF files.
ref.genome	A ref.genome argument as described in ICAMS .
trans.ranges	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
region	A character string designating a genomic region; see as.catalog and ICAMS .
output.file	The name of the PDF file to be produced.

Details

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

Value

A list of 3 SBS catalogs (one each for 96, 192, and 1536), 3 DBS catalogs (one each for 78, 136, and 144), Indel catalog and their graphs plotted to PDF with specified file name. If trans.ranges = NULL, SBS 192 and DBS 144 catalog will not be generated and plotted. Each catalog has attributes added. See [as.catalog](#) for more details.

Note

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

Examples

```
file <- c(system.file("extdata",
  "Mutect.GRCh37.vcf",
  package = "ICAMS"))

catalogs <-
  MutectVCFFilesToCatalogAndPlotToPdf(file, ref.genome = "hg19",
    trans.ranges = trans.ranges.GRCh37,
    region = "genome",
    output.file = file.path(tempdir(), "Mutect.pdf"))
```

PlotCatalog	<i>Plot one spectrum or signature.</i>
-------------	---

Description

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

Usage

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

Arguments

catalog	A catalog as defined in ICAMS with attributes added. See as.catalog for more details.
plot.SBS12	Only meaningful for class SBS192Catalog; if TRUE, generate an abbreviated plot of only SBS without context, i.e. C>A, C>G, C>T, T>A, T>C, T>G each on transcribed and untranscribed strands, rather than SBS in trinucleotide context, e.g. ACA > AAA, ACA > AGA, ..., TCT > TAT, ...
cex	A numerical value giving the amount by which mutation class labels, mutation counts(if it exists), y axis and its labels, x axis labels and its annotations(if it exists), sample name and legend(if it exists) should be magnified relative to the default. Only implemented for SBS96Catalog, SBS192Catalog and DBS144Catalog.
grid	A logical value indicating whether to draw grid lines. Only implemented for SBS96Catalog.
upper	A logical value indicating whether to draw horizontal lines and the names of major mutation class on top of graph. Only implemented for SBS96Catalog.
xlabel	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog.

Value

invisible(TRUE)

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 they range from 1 to 6+.

Examples

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file, ref.genome = "hg19",
                        region = "genome",
                        catalog.type = "counts")
colnames(catSBS96) <- "sample"
PlotCatalog(catSBS96)
```

PlotCatalogToPdf	<i>Plot catalog to a PDF file.</i>
------------------	------------------------------------

Description

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

Usage

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

Arguments

catalog	A catalog as defined in ICAMS with attributes added. See as.catalog for more details.
file	The name of the PDF file to be produced.
plot.SBS12	Only meaningful for class SBS192Catalog; if TRUE, generate an abbreviated plot of only SBS without context, i.e. C>A, C>G, C>T, T>A, T>C, T>G each on transcribed and untranscribed strands, rather than SBS in trinucleotide context, e.g. ACA > AAA, ACA > AGA, ..., TCT > TAT, ... There are 12 bars in the graph.
cex	A numerical value giving the amount by which mutation class labels, mutation counts(if it exists), y axis and its labels, x axis labels and its annotations(if it exists), sample name and legend(if it exists) should be magnified relative to the default. Only implemented for SBS96Catalog, SBS192Catalog and DBS144Catalog.
grid	A logical value indicating whether to draw grid lines. Only implemented for SBS96Catalog.
upper	A logical value indicating whether to draw horizontal lines and the names of major mutation class on top of graph. Only implemented for SBS96Catalog.
xlabels	A logical value indicating whether to draw x axis labels. Only implemented for SBS96Catalog.

Value

invisible(TRUE)

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 they range from 1 to 6+.

Examples

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file, ref.genome = "hg19",
                       region = "genome",
                       catalog.type = "counts")
colnames(catSBS96) <- "sample"
PlotCatalogToPdf(catSBS96, file = file.path(tempdir(), "test.pdf"))
```

ReadAndSplitMutectVCFs

Read and split Mutect VCF files.

Description

Read and split Mutect VCF files.

Usage

```
ReadAndSplitMutectVCFs(files)
```

Arguments

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

Value

A list with 3 in-memory VCFs and two left-over VCF-like data frames with rows that were not incorporated into the first 3 VCFs, as follows:

1. SBS VCF with only single base substitutions.
2. DBS VCF with only doublet base substitutions as called by Mutect.
3. ID VCF with only small insertions and deletions.
4. `other.subs` VCF like `data.frame` with rows for coordinate substitutions involving 3 or more nucleotides, e.g. ACT > TGA or AACT > GGTA.
5. `multiple.alternative.alleles` VCF like `data.frame` with rows for variants with multiple alternative alleles, for example ACT mutated to both AGT and ACT at the same position.

See Also

[MutectVCFFilesToCatalog](#)

Examples

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

ReadAndSplitStrelkaSBSVCFs

Read and split Strelka SBS VCF files.

Description

Read and split Strelka SBS VCF files.

Usage

```
ReadAndSplitStrelkaSBSVCFs(files)
```

Arguments

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

Value

A list of 3 in-memory objects as follows:

1. `SBS.vcfs` List of data.frames of pure SBS mutations – no DBS or 3+BS mutations.
2. `DBS.vcfs` List of data.frames of pure DBS mutations – no SBS or 3+BS mutations.
3. `ThreePlus` List of data.tables with the key `CHROM`, `LOW.POS`, `HIGH.POS`. containing rows that that in the input that did not represent SBSs or DBSs.

See Also

[StrelkaSBSVCFFilesToCatalog](#)

Examples

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

ReadCatalog

Read catalog.

Description

Read a catalog in standardized format from path.

Usage

```
ReadCatalog(file, ref.genome, region, catalog.type, strict = TRUE)
```


Arguments

<code>file</code>	Path to a catalog on disk in the standardized format.
<code>ref.genome</code>	A <code>ref.genome</code> argument as described in ICAMS .
<code>region</code>	region A character string designating a genomic region; see as.catalog and ICAMS .
<code>catalog.type</code>	One of "counts", "density", "counts.signature", "density.signature".
<code>strict</code>	If TRUE, do additional checks on the input, and stop if the checks fail.

Details

See also [WriteCatalog](#)

Value

A catalog as an S3 object; see [as.catalog](#).

Note

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

Examples

```
file <- system.file("extdata",
                    "strelka.regress.cat.sbs.96.csv",
                    package = "ICAMS")
catSBS96 <- ReadCatalog(file, ref.genome = "hg19",
                        region = "genome",
                        catalog.type = "counts")
```

ReadStrelkaIDVCFs	<i>Read Strelka ID (insertion and deletion) VCF files.</i>
-------------------	--

Description

Read Strelka ID (insertion and deletion) VCF files.

Usage

```
ReadStrelkaIDVCFs(files)
```

Arguments

<code>files</code>	Character vector of file paths to the VCF files.
--------------------	--

Value

A list of vcfs from files.

Note

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

See Also

[StrelkaIDVCFFilesToCatalog](#)

Examples

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

revc	<i>Reverse complement every string in string.vec.</i>
------	---

Description

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

Usage

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

Arguments

string.vec A character vector.

Value

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

Examples

```
revc("aTgc") # GCAT

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

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

`StrelkaIDVCFFilesToCatalog`*Create ID (indel) catalog from Strelka ID VCF files*

Description

Create ID (indel) catalog from the Strelka ID VCFs specified by files

Usage

```
StrelkaIDVCFFilesToCatalog(files, ref.genome, region = "unknown")
```

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 ICAMS .
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .

Details

This function calls [VCFsToIDCatalogs](#)

Value

An ID (indel) catalog with attributes added. See [as.catalog](#) for more details.

Note

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

Examples

```
file <- c(system.file("extdata",  
                     "Strelka.ID.GRCh37.vcf",  
                     package = "ICAMS"))  
catID <- StrelkaIDVCFFilesToCatalog(file, ref.genome = "hg19",  
                                   region = "genome")
```

`StrelkaIDVCFFilesToCatalogAndPlotToPdf`*Create ID (indel) catalog from Strelka ID VCF files and plot them to PDF*

Description

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

Usage

```
StrelkaIDVCFFilesToCatalogAndPlotToPdf(files, ref.genome,
  region = "unknown", output.file)
```

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 ICAMS .
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .
<code>output.file</code>	The name of the PDF file to be produced.

Details

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

Value

An ID (indel) catalog and its graph plotted to PDF with specified file name. The ID (indel) catalog has attributes added. See [as.catalog](#) for more details.

Note

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

Examples

```
file <- c(system.file("extdata",
  "Strelka.ID.GRCh37.vcf",
  package = "ICAMS"))
catID <-
  StrelkaIDVCFFilesToCatalogAndPlotToPdf(file, ref.genome = "hg19",
    region = "genome",
    output.file = file.path(tempdir(),
      "StrelkaID.pdf"))
```

StrelkaSBSVCFFilesToCatalog

Create SBS and DBS catalogs from Strelka SBS VCF files.

Description

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

Usage

```
StrelkaSBSVCFFilesToCatalog(files, ref.genome, trans.ranges = NULL,
  region = "unknown")
```

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 ICAMS .
<code>trans.ranges</code>	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .

Details

This function calls [VCFsToSBSCatalogs](#) and [VCFsToDBSCatalogs](#).

Value

A list of 3 SBS catalogs (one each for 96, 192, and 1536) and 3 DBS catalogs (one each for 78, 136, and 144). If `trans.ranges = NULL`, 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 catalog only contains mutations in transcribed regions.

Examples

```
file <- c(system.file("extdata",
                     "Strelka.SBS.GRCh37.vcf",
                     package = "ICAMS"))
catalogs <- StrelkaSBSVCFFilesToCatalog(file, ref.genome = "hg19",
                                       trans.ranges = trans.ranges.GRCh37,
                                       region = "genome")
```

StrelkaSBSVCFFilesToCatalogAndPlotToPdf

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

Description

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

Usage

```
StrelkaSBSVCFFilesToCatalogAndPlotToPdf(files, ref.genome,
                                       trans.ranges = NULL, region = "unknown", output.file)
```

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 ICAMS .
<code>trans.ranges</code>	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .
<code>output.file</code>	The name of the PDF file to be produced.

Details

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

Value

A list of 3 SBS catalogs (one each for 96, 192, and 1536), 3 DBS catalogs (one each for 78, 136, and 144) and their graphs plotted to PDF with specified file name. If `trans.ranges = NULL`, SBS 192 and DBS 144 catalog will not be generated and plotted. Each catalog has attributes added. See [as.catalog](#) for more details.

Note

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

Examples

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

catalogs <-
  StrelkaSBSVCFFilesToCatalogAndPlotToPdf(file, ref.genome = "hg19",
                                           trans.ranges = trans.ranges.GRCh37,
                                           region = "genome",
                                           output.file = file.path(tempdir(),
                                                                    "StrelkaSBS.pdf"))
```

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, gene.name. It uses one-based coordinates.

Details

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

trans.ranges.GRCh37: **Human** GRCh37.

trans.ranges.GRCh38: **Human** GRCh38.

trans.ranges.GRCm38: **Mouse** GRCm38.

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

This information is needed for [StrelkaSBSVCFFilesToCatalog](#), [StrelkaSBSVCFFilesToCatalogAndPlotToPdf](#), [MutectVCFFilesToCatalog](#), [MutectVCFFilesToCatalogAndPlotToPdf](#), [VCFsToSBSCatalogs](#) and [VCFsToDBSCatalogs](#).

Source

ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_human/release_30/GRCh37_mapping/gencode.v30lift37.annotation.gff3.gz

ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_human/release_30/gencode.v30.annotation.gff3.gz

ftp://ftp.ebi.ac.uk/pub/databases/gencode/Gencode_mouse/release_M21/gencode.vM21.annotation.gff3.gz

Examples

```
trans.ranges.GRCh37
# chrom    start      end strand gene.name
#    1      65419    71585      +    OR4F5
#    1     367640   368634      +    OR4F29
#    1     621059   622053      -    OR4F16
#    1     859308   879961      +    SAMD11
#    1     879583   894689      -    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

<code>catalog</code>	An SBS or DBS catalog as described in ICAMS ; must not be an ID (indel) catalog.
<code>target.ref.genome</code>	A <code>ref.genome</code> argument as described in ICAMS . If NULL, then defaults to the <code>ref.genome</code> attribute of catalog.
<code>target.region</code>	A region argument; see as.catalog and ICAMS . If NULL, then defaults to the <code>region</code> attribute of catalog.
<code>target.catalog.type</code>	A character string acting as a catalog type identifier, one of "counts", "density", "counts.signature", "density.signature"; see as.catalog . If NULL, then defaults to the <code>catalog.type</code> attribute of catalog.
<code>target.abundance</code>	A vector of counts different source K-mer sequences for mutations. See all.abundance . If NULL, then the function attempt to infer the <code>target.abundance</code> from the class of catalog and the values of the <code>target.ref.genome</code> , <code>target.region</code> , and <code>target.catalog.type</code> . It is an error if the inferred abundance is different from a non-NULL <code>target.abundance</code> .

Details

Only the following transformations are legal:

1. counts -> counts (used to transform between the source abundance and `target.abundance`)
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](#).

Examples

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

```

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, trans.ranges = NULL,
                    region = "unknown")

```

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 ICAMS .
<code>trans.ranges</code>	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .

Value

A list of 3 DBS catalogs, one each for 78, 144, 136: `catDBS78 catDBS144 catDBS136`. If `trans.ranges = NULL`, DBS 144 catalog will not be generated. Each catalog has attributes added. See [as.catalog](#) for more details.

Note

DBS 144 catalog only contains mutations in transcribed regions.

Examples

```

file <- c(system.file("extdata",
                      "Mutect.GRCh37.vcf",
                      package = "ICAMS"))
list.of.DBS.vcfs <- ReadAndSplitMutectVCFs(file)$DBS
catalogs.DBS <- VCFsToDBSCatalogs(list.of.DBS.vcfs, ref.genome = "hg19",
                                trans.ranges = trans.ranges.GRCh37,
                                region = "genome")

```

VCFsToIDCatalogs	<i>Create ID (insertion and deletion) catalog from ID VCFs</i>
------------------	--

Description

Create ID (insertion and deletion) catalog from ID VCFs

Usage

```
VCFsToIDCatalogs(list.of.vcfs, ref.genome, region = "unknown")
```

Arguments

<code>list.of.vcfs</code>	List of in-memory 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 ICAMS .
<code>region</code>	A character string acting as a region identifier, one of "genome", "exome".

Value

An S3 object containing an ID (indel) catalog with class "catalog". See [as.catalog](#) for more details.

Examples

```
file <- c(system.file("extdata",
                      "Mutect.GRCh37.vcf",
                      package = "ICAMS"))
list.of.ID.vcfs <- ReadAndSplitMutectVCFs(file)$ID
catID <- VCFsToIDCatalogs(list.of.ID.vcfs, ref.genome = "hg19",
                          region = "genome")
```

VCFsToSBSCatalogs	<i>Create SBS catalogs from SBS VCFs</i>
-------------------	--

Description

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

Usage

```
VCFsToSBSCatalogs(list.of.SBS.vcfs, ref.genome, trans.ranges = NULL,
                  region = "unknown")
```

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 ICAMS .
<code>trans.ranges</code>	a data.table which contains transcript range and strand information. Please refer to TranscriptRanges for more details.
<code>region</code>	A character string designating a genomic region; see as.catalog and ICAMS .

Value

A list of 3 SBS catalogs, one each for 96, 192, 1536: `catSBS96 catSBS192 catSBS1536`. If `trans.ranges = NULL`, SBS 192 catalog will not be generated. Each catalog has attributes added. See [as.catalog](#) for more details.

Note

SBS 192 catalogs only contain mutations in transcribed regions.

Examples

```
file <- c(system.file("extdata",
                     "Mutect.GRCh37.vcf",
                     package = "ICAMS"))
list.of.SBS.vcfs <- ReadAndSplitMutectVCFs(file)$SBS
catalogs.SBS <- VCFsToSBSCatalogs(list.of.SBS.vcfs, ref.genome = "hg19",
                                trans.ranges = trans.ranges.GRCh37,
                                region = "genome")
```

WriteCatalog

Write a catalog

Description

Write a catalog to a file.

Usage

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

Arguments

<code>catalog</code>	A catalog as defined in ICAMS ; see also as.catalog .
<code>file</code>	The path to the file to be created.
<code>strict</code>	If TRUE, do additional checks on the input, and stop if the checks fail.

Details

See also [ReadCatalog](#).

Note

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

Examples

```
file <- system.file("extdata",  
                    "strelka.regress.cat.sbs.96.csv",  
                    package = "ICAMS")  
catSBS96 <- ReadCatalog(file, ref.genome = "hg19",  
                        region = "genome",  
                        catalog.type = "counts")  
WriteCatalog(catSBS96, file = file.path(tempdir(), "catSBS96.csv"))
```

Index

*Topic **datasets**

all.abundance, [2](#)
CatalogRowOrder, [4](#)
TranscriptRanges, [22](#)

all.abundance, [2](#), [3](#), [9](#), [10](#), [24](#)
as.catalog, [3](#), [8](#), [9](#), [11–14](#), [17](#), [19–22](#), [24–27](#)
available.genomes, [10](#)

BSgenome, [9](#)
BSgenome.Hsapiens.1000genomes.hs37d5, [9](#)
BSgenome.Hsapiens.UCSC.hg38, [9](#)
BSgenome.Mmusculus.UCSC.mm10, [9](#), [10](#)

catalog.row.order (CatalogRowOrder), [4](#)
CatalogRowOrder, [3](#), [4](#), [11](#)
Collapse144CatalogTo78
(CollapseCatalog), [4](#)
Collapse1536CatalogTo96
(CollapseCatalog), [4](#)
Collapse192CatalogTo96
(CollapseCatalog), [4](#)
CollapseCatalog, [4](#), [10](#)

data.table, [11](#), [12](#), [21–23](#), [25](#), [27](#)

FindDelMH, [5](#)

GetMutectVAF (GetVAF), [7](#)
GetStrelkaVAF (GetVAF), [7](#)
GetVAF, [7](#)

ICAMS, [3](#), [5](#), [8](#), [11–14](#), [17](#), [19–22](#), [24–27](#)
ICAMS-package (ICAMS), [8](#)

MutectVCFFilesToCatalog, [9](#), [11](#), [12](#), [15](#), [23](#)
MutectVCFFilesToCatalogAndPlotToPdf, [12](#), [23](#)

PlotCatalog, [9](#), [13](#)
PlotCatalogToPdf, [9](#), [12](#), [14](#), [20](#), [22](#)

ReadAndSplitMutectVCFs, [15](#)
ReadAndSplitStrelkaSBSVCFs, [16](#)

ReadCatalog, [9](#), [10](#), [16](#), [27](#)
ReadStrelkaIDVCFs, [17](#)
revc, [18](#)
reverseComplement, [18](#)

StrelkaIDVCFFilesToCatalog, [9](#), [18](#), [19](#)
StrelkaIDVCFFilesToCatalogAndPlotToPdf, [19](#)
StrelkaSBSVCFFilesToCatalog, [9](#), [16](#), [20](#), [22](#), [23](#)
StrelkaSBSVCFFilesToCatalogAndPlotToPdf, [9](#), [21](#), [23](#)

trans.ranges.GRCh37 (TranscriptRanges), [22](#)
trans.ranges.GRCh38 (TranscriptRanges), [22](#)
trans.ranges.GRCm38 (TranscriptRanges), [22](#)

TranscriptRanges, [11](#), [12](#), [21](#), [22](#), [22](#), [25](#), [27](#)
TransformCatalog, [8](#), [10](#), [13](#), [14](#), [23](#)

VCFsToDBSCatalogs, [11](#), [21](#), [23](#), [25](#)
VCFsToIDCatalogs, [11](#), [19](#), [20](#), [26](#)
VCFsToSBSCatalogs, [11](#), [21](#), [23](#), [26](#)

WriteCatalog, [10](#), [17](#), [27](#)