

Package ‘ICAMS’

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Type Package

Title In-depth Characterization and Analysis of Mutational Signatures

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Description This package has functions to read in VCF files from Strelka and Mutect (in the Broad GATK package), create, read, and write single nucleotide substitutions (SNS), double nucleotide substitutions (DNS), insertions and deletions (ID) catalogs and do different types of plotting.
This alpha version only works with VCFs for human GRCh37, but will work for arbitrary human catalogs (assuming no major change in ``opportunities" between GRCh37 and GRCh38).

License GPL-3

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GenomicRanges,
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'INDELS_related_functions.R'
'utility_functions.R'
'VCF_to_catalog_functions.R'
'data.R'
'plot.R'
'read_write_catalog.R'
'test_functions.R'

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CatalogRowOrder	<i>Canonical order of row names in a catalog</i>
-----------------	--

Description

Canonical order of row names in a catalog

Usage

catalog.row.order

Format

A list which contains string of characters indicating the canonical order of row names in a catalog.

Note

In the ID (insertion and deletion) catalog, deletion repeat size ranges from 0 to 5+, but for plotting and end user documentation it ranges from 1 to 6+.

CollapseCatalog	<i>Collapse catalog functions</i>
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Description

Collapse a catalog matrix

Usage

```
Collapse192To96(catalog)
```

```
Collapse1536To96(catalog)
```

```
Collapse144To78(catalog)
```

Arguments

catalog	A catalog matrix to be collapsed whose row names indicate the mutation types while its columns show the occurrences of each mutation type of different samples.
---------	---

Details

Collapse192To96 Collapse a SNS 192 catalog matrix to a SNS 96 catalog matrix.

Collapse1536To96 Collapse a SNS 1536 catalog matrix to a SNS 96 catalog matrix.

Collapse144To78 Collapse a DNS 144 catalog matrix to a DNS 78 catalog matrix.

Value

A canonical catalog matrix whose row names indicate the mutation types while its columns show the occurrences of each mutation type of different samples.

FindDelMH	<i>Return the length of microhomology at a deletion</i>
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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 so that the logic behind it will be documented for users.

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
```

The deletion caller 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

```
TODO(Steve): add check in code
GACTAG----TT GACTAGTT GACTAG[CTAG]TT
          ***** ----
```

```
GACT----AGTT GACTAGTT GACT[AGCT]AGTT
          ** ----
```

But the function only flags this with a -1 return; it does not figure out the repeat extent.

In the implementation, the function finds:

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

GetVAF	<i>Extract the VAFs (variant allele frequencies) from a VCF file.</i>
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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`.

Description

This package has functions to read in VCF files from Strelka and Mutect (in the Broad GATK package), create, read, and write single nucleotide substitutions (SNS), double nucleotide substitutions (DNS), insertions and deletions (ID) catalogs and do different types of plotting.

Details

This alpha version only works with VCFs for human GRCh37, but will work for arbitrary **human** catalogs (assuming no major change in "opportunities" between GRCh37 and GRCh38).

Reading and splitting VCF files

1. [ReadAndSplitStrelkaSNSVCFs](#) Read and split Strelka single nucleotide substitution (SNS) VCFs (not Strelka indel VCFs).
2. [ReadStrelkaIDVCFs](#) Read Strelka indel (ID) VCFs (not Strelka SNS VCFs).
3. [ReadAndSplitMutectVCFs](#) Read and split Mutect VCFs, which contain indels and double nucleotide substitutions (DNSs) as well and SNSs.

Creating catalogs from VCF files

1. [StrelkaSNSVCFFilesToCatalog](#), which creates 3 SNS catalogs (96, 192, 1536) and 3 DNS catalogs (78, 136, 144) from the Strelka SNS VCFs.
2. [StrelkaIDVCFFilesToCatalog](#), which creates ID (indels) catalog from the Strelka ID VCFs.
3. [MutectVCFFilesToCatalog](#), which creates 3 SNS catalogs (96, 192, 1536), 3 DNS catalogs (78, 136, 144) and ID (indels) catalog from the Mutect VCFs.

Reading catalogs

Functions for reading files that contain mutational spectrum catalogs in standardized format. These also work for reading mutational signature profiles. [ReadCatalog](#)

Writing catalogs

Functions for writing a mutational spectrum catalog to a file on disk. These also work for writing mutational signature profiles. [WriteCatalog](#)

Transforming catalogs

Functions for transforming count spectra from a particular organism region to an inferred count spectra based on the target nucleotide abundance. [TransformSpectra](#)

Collapsing catalogs

Functions for collapsing a mutation catalog. [CollapseCatalog](#)

Plotting catalogs

Functions for plotting mutation spectrum catalogs to a PDF file. These also work for plotting mutational signature profiles. [PlotCatalogToPdf](#)

Exported data

1. [CatalogRowOrder](#) Canonical order of row names in a catalog.
2. [TranscriptRanges](#) Transcript ranges and strand information for a particular organism.

MutectVCFFilesToCatalog

Create SNS and DNS catalogs from Mutect VCF files

Description

Create 3 SNS catalogs (96, 192, 1536) and 3 DNS catalogs (78, 136, 144) from the Mutect VCFs specified by `vector.of.file.paths`

Usage

```
MutectVCFFilesToCatalog(vector.of.file.paths, genome, trans.ranges)
```

Arguments

<code>vector.of.file.paths</code>	A vector containing the paths of the Mutect VCF files.
<code>genome</code>	Name of a particular reference genome (without quotations marks).
<code>trans.ranges</code>	A data.table which contains transcript range and strand information.

Details

This function calls [VCFsToNSCatalogs](#), [VCFsToDNSCatalogs](#) and [VCFsToIDCatalogs](#)

Value

A list of 3 SNS catalogs (one each for 96, 192, and 1536) , 3 DNS catalogs (one each for 78, 136, and 144) and ID catalog.

PlotCatalogToPdf	<i>Plot catalog to pdf functions</i>
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Description

Plot mutation catalogs of various samples to a PDF file

Usage

```
PlotCatSNS96ToPdf(catalog, name, id = colnames(catalog),
  type = "density", grid = FALSE, upper = TRUE, xlabel = TRUE,
  abundance = NULL)
```

```
PlotCatSNS192ToPdf(catalog, name, id = colnames(catalog),
  type = "counts", cex = 0.8, abundance = NULL)
```

```
PlotCatSNS192StrandToPdf(catalog, name, id = colnames(catalog),
  type = "counts", cex = 1, abundance = NULL)
```

```
PlotCatSNS1536ToPdf(catalog, name, id = colnames(catalog), abundance)
```

```
PlotCatDNS78ToPdf(catalog, name, id = colnames(catalog),
  type = "density", abundance = NULL)
```

```
PlotCatDNS144ToPdf(catalog, name, id = colnames(catalog),
  type = "counts", cex = 1, abundance = NULL)
```

```
PlotCatDNS136ToPdf(catalog, name, id = colnames(catalog),
  type = "density", abundance = NULL)
```

```
PlotCatIDToPdf(catalog, name, id = colnames(catalog), type = "counts")
```

Arguments

catalog	A matrix of mutation counts. Rownames indicate the mutation types. Each column contains the mutation counts for one sample.
name	The name of the PDF file to be produced.
id	A vector containing the identifiers of the samples in catalog.
type	A vector of values indicating the type of plot for each sample. If type = "counts", the graph will plot the occurrences of the mutation types in the sample. If type = "signature", the graph will plot mutation signatures of the sample. If type = "density", the graph will plot the rates of mutations per million nucleotides for each mutation type. (Please take note there is no "density" type for PlotCatIDToPdf function and the option of type = "density" is not implemented for function PlotCatSNS192ToPdf, PlotCatSNS192StrandToPdf and PlotCatDNS144ToPdf at the current stage.)
grid	If TRUE, draw grid lines in the graph.
upper	If TRUE, draw horizontal lines and the names of major mutation class on top of graph.

xlabels	If TRUE, draw x axis labels.
abundance	A single column matrix, see Abundance , used only when type = "density".
cex	A numerical value giving the amount by which mutation class labels, y axis labels, sample name and legend (if it exists) should be magnified relative to the default.

Details

PlotCatSNS96ToPdf Plot the SNS 96 mutation catalog of various samples to a PDF file.

PlotCatSNS192ToPdf Plot the SNS 192 mutation catalog of various samples to a PDF file.

PlotCatSNS192StrandToPdf Plot the transcription strand bias graph of 6 SNS mutation types ("C>A", "C>G", "C>T", "T>A", "T>C", "T>G") of various samples to a PDF file.

PlotCatSNS1536ToPdf Plot the 1536 mutation catalog of ≥ 1 samples to a PDF file. The mutation types are in six-letters like CATTAT, first 2-letters CA refers to (-2, -1) position, third letter T refers to the base which has mutation, next second 2-letters TA refers to (+1, +2) position, last letter T refers to the base after mutation.

PlotCatDNS78ToPdf Plot the DNS 78 mutation catalog of various samples to a PDF file.

PlotCatDNS144ToPdf Plot the transcription strand bias graph of 10 major DNS mutation types ("AC>NN", "AT>NN", "CC>NN", "CG>NN", "CT>NN", "GC>NN", "TA>NN", "TC>NN", "TG>NN", "TT>NN") of various samples to a PDF file.

PlotCatDNS136ToPdf Plot the tetranucleotide sequence contexts of 10 major DNS mutation types ("AC>NN", "AT>NN", "CC>NN", "CG>NN", "CT>NN", "GC>NN", "TA>NN", "TC>NN", "TG>NN", "TT>NN") of various samples to a PDF file.

PlotCatIDToPdf Plot the insertion and deletion catalog of various samples to a PDF file. (Please take note that deletion repeat size ranges from 0 to 5+ in the catalog, but for plotting and end user documentation it ranges from 1 to 6+.)

Value

invisible(TRUE)

ReadAndSplitMutectVCFs

Read and split Mutect VCF files from paths

Description

Read and split Mutect VCF files from paths

Usage

```
ReadAndSplitMutectVCFs(vector.of.file.paths)
```

Arguments

vector.of.file.paths

A vector containing the paths of the 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. SNS VCF with only single nucleotide substitutions.
2. DNS VCF with only doublet nucleotide 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.

ReadAndSplitStrelkaSNSVCFs

Read and split Strelka SNS VCF files from paths

Description

Read and split Strelka SNS VCF files from paths

Usage

```
ReadAndSplitStrelkaSNSVCFs(vector.of.file.paths)
```

Arguments

```
vector.of.file.paths
```

A vector containing the paths of the VCF files.

Value

A list of 3 in-memory objects with the elements: `SNS.vcfs`: List of Data frames of pure SNS mutations – no DNS or 3+BS mutations `DNS.vcfs`: List of Data frames of pure DNS mutations – no SNS or 3+BS mutations `ThreePlus`: List of Data tables with the key `CHROM`, `LOW.POS`, `HIGH.POS` and additional information (reference sequence, alternative sequence, context, etc.) Additional information not fully implemented at this point because of limited immediate biological interest.

ReadCatalog

Read Catalog Functions

Description

Read a catalog in standardized format from path

Usage

```
ReadCatSNS96(path, strict = TRUE)
```

```
ReadCatSNS192(path, strict = TRUE)
```

```
ReadCatSNS1536(path, strict = TRUE)
```

```
ReadCatDNS78(path, strict = TRUE)
```

```
ReadCatDNS144(path, strict = TRUE)
```

```
ReadCatDNS136(path, strict = TRUE)
```

```
ReadCatID(path, strict = TRUE)
```

Arguments

`path` Path to a catalog on disk in the standardized format.

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

Details

`ReadCatSNS96` Read a 96 SNS catalog from path

`ReadCatSNS192` Read a 192 SNS catalog from path

`ReadCatSNS1536` Read a 1536 SNS catalog from path

`ReadCatDNS78` Read a 78 DNS catalog from path

`ReadCatDNS144` Read a 144 DNS catalog from path

`ReadCatDNS136` Read a 136 DNS catalog from path

`ReadCatID` Read a ID (insertion/deletion) catalog from path Please take note that deletion repeat size ranges from 0 to 5+ in the catalog, but for plotting and end user documentation it ranges from 1 to 6+.

See also [WriteCatalog](#)

Value

A catalog in canonical in-memory format.

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

Description

Read Strelka ID (insertion and deletion) VCF files from paths

Usage

```
ReadStrelkaIDVCFs(vector.of.file.paths)
```

Arguments

```
vector.of.file.paths
```

A vector containing the paths of the VCF files.

Value

A list of vcfs from vector.of.file.paths.

Note

In the ID (insertion and deletion) catalog, deletion repeat size ranges from 0 to 5+, but for plotting and end user documentation it ranges from 1 to 6+.

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

Description

Reverse complement every string in string.vec.

Usage

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

Arguments

```
string.vec
```

a vector of type character.

Value

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

StrelkaIDVCFFilesToCatalog

Create ID (indel) catalog from Strelka ID VCF files

Description

Create ID (indel) catalog from the Strelka ID VCFs specified by vector.of.file.paths

Usage

```
StrelkaIDVCFFilesToCatalog(vector.of.file.paths, genome)
```

Arguments

vector.of.file.paths

A vector containing the paths of the Strelka ID VCF files.

genome

Name of a particular reference genome (without quotations marks).

Details

This function calls [VCFsToIDCatalogs](#)

Value

An ID (indel) catalog

Note

In the ID (insertion and deletion) catalog, deletion repeat size ranges from 0 to 5+, but for plotting and end user documentation it ranges from 1 to 6+.

StrelkaSNSVCFFilesToCatalog

Create SNS and DNS catalogs from Strelka SNS VCF files

Description

Create 3 SNS catalogs (96, 192, 1536) and 3 DNS catalogs (78, 136, 144) from the Strelka SNS VCFs specified by vector.of.file.paths

Usage

```
StrelkaSNSVCFFilesToCatalog(vector.of.file.paths, genome, trans.ranges)
```

Arguments

vector.of.file.paths

A vector containing the paths of the Strelka SNS VCF files.

genome

Name of a particular reference genome (without quotations marks).

trans.ranges

A data.table which contains transcript range and strand information.

Details

This function calls [VCFsToNSCatalogs](#) and [VCFsToDNSCatalogs](#)

Value

A list of 3 SNS catalogs (one each for 96, 192, and 1536) and 3 DNS catalogs (one each for 78, 136, and 144)

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

Description

Transcript ranges and strand information for a particular organism

Usage

```
trans.ranges.GRCh37
```

```
old.trans.ranges.GRCh37
```

```
trans.ranges.GRCh38
```

Format

A data.table which contains transcript range and strand information for a particular organism.

Details

`trans.ranges.GRCh37` A data.table which contains transcript range and strand information for **Human** GRCh37. It is derived from a raw **GFF3** format file, from which only the following four gene types are kept to facilitate transcriptional strand bias analysis: `protein_coding`, `retained_intron`, `processed_transcript` and `nonsense_mediated_decay`. It contains chromosome name, start, end position, strand information and gene name and is keyed by `chrom`, `chromStart`, and `chromEnd`. It can be used in function [StrelkaSNSVCFFilesToCatalog](#).

`trans.ranges.GRCh38` A data.table which contains transcript range and strand information for **Human** GRCh38. It is derived from a raw **GFF3** format file, from which only the following four gene types are kept to facilitate transcriptional strand bias analysis: `protein_coding`, `retained_intron`, `processed_transcript` and `nonsense_mediated_decay`. It contains chromosome name, start, end position, strand information and gene name and is keyed by `chrom`, `chromStart`, and `chromEnd`. It can be used in function [StrelkaSNSVCFFilesToCatalog](#).

`old.trans.ranges.GRCh37` A data.table which contains transcript range and strand information for **Human** GRCh37, which is derived from a raw **BED** format file and is keyed by `chrom`, `chromStart`, and `chromEnd`. This is mostly for testing purpose, may be removed in the future.

Description

Write a mutation catalog to a file on disk

Usage

```
WriteCatSNS96(ct, path, strict = TRUE)
```

```
WriteCatSNS192(ct, path, strict = TRUE)
```

```
WriteCatSNS1536(ct, path, strict = TRUE)
```

```
WriteCatDNS78(ct, path, strict = TRUE)
```

```
WriteCatDNS144(ct, path, strict = TRUE)
```

```
WriteCatDNS136(ct, path, strict = TRUE)
```

```
WriteCatID(ct, path, strict = TRUE)
```

Arguments

ct	A matrix of mutation catalog.
path	The path of the file to be written on disk.
strict	If TRUE, do additional checks on the input, and stop if the checks fail.

Details

WriteCatSNS96 Write a SNS 96 mutation catalog to a file on disk

WriteCatSNS192 Write a SNS 192 mutation catalog to a file on disk

WriteCatSNS1536 Write a SNS 1536 mutation catalog to a file on disk

WriteCatDNS78 Write a DNS 78 mutation catalog to a file on disk

WriteCatDNS144 Write a DNS 144 mutation catalog to a file on disk

WriteCatDNS136 Write a 136 DNS catalog from path

WriteCatID Write a ID (insertion/deletion) catalog to a file on disk Please take note that deletion repeat size ranges from 0 to 5+ in the catalog, but for plotting and end user documentation it ranges from 1 to 6+.

See also [ReadCatalog](#)

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