Package ‘YAPSA’

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Description This package provides functions and routines for supervised analyses of mutational signatures (i.e., the signatures have to be known, cf. L. Alexandrov et al., Nature 2013 and L. Alexandrov et al., Bioaxiv 2018). In particular, the family of functions LCD (LCD = linear combination decomposition) can use optimal signature-specific cutoffs which takes care of different detectability of the different signatures. Moreover, the package provides different sets of mutational signatures, including the COSMIC and PCAWG SNV signatures and the PCAWG Indel signatures; the latter inferring that with YAPSA, the concept of supervised analysis of mutational signatures is extended to Indel signatures. YAPSA also provides confidence intervals as computed by profile likelihoods and can perform signature analysis on a stratified mutational catalogue (SMC = stratify mutational catalogue) in order to analyze enrichment and depletion patterns for the signatures in different strata.

License GPL-3

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**add_annotation**

Add information to an annotation data structure

**Description**

Function to iteratively add information to an annotation data structure as needed for HeatmapAnnotation and especially for annotation_exposures_barplot

**Usage**

```r
add_annotation(
    in_annotation_col,
    in_annotation_df,
    in_attribution_vector,
    in_colour_vector,
    in_name
)
```
Arguments

in_annotation_col
List, every element of which refers to one layer of annotation. List elements are structures corresponding to named colour vectors.

in_annotation_df
Data frame, every column of which corresponds to a layer of annotation. It has as many rows as there are samples, every entry in a row corresponding to the attribute the samples has for the corresponding layer of annotation. The factor levels of a column of `in_annotation_df` correspond to the names of the corresponding element in `in_annotation_col`.

in_attrtribution_vector
A vector which is going to be cbinded to `in_annotation_df`, carrying the annotation information of the new layer to be added.

in_colour_vector
Named vector of colours to be attributed to the new annotation.

in_name
Name of the new layer of annotation.

Value

A list with entries

- `annotation_col`: A list as in `in_annotation_col` but with one additional layer of annotation.
- `annotation_df`: A data frame as in `in_annotation_df` but with one additional layer of annotation.

Examples

NULL

---

add_as_fist_to_list  Add an element as first entry to a list

Description

Works for all types of lists and inputs.

Usage

add_as_fist_to_list(in_list, in_element)

Arguments

in_list  List to which an element is to be added
in_element  Element to be added
aggregate_exposures_by_category

Aggregate exposures by category

Description

If a valid category (i.e. it matches to a category specified in in_sig_ind_df) is supplied, then the exposures are aggregated over this category.

Usage

aggregate_exposures_by_category(in_exposures_df, in_sig_ind_df, in_category)

Arguments

- **in_exposures_df**: Input data frame of exposures.
- **in_sig_ind_df**: Input data frame of meta information on the signatures. Has to match the signatures in in_exposures_df.
- **in_category**: Category to be aggregated over.

Value

A list with entries:

- **exposures**: The exposures \( H \), a numeric data frame with \( l \) rows and \( m \) columns, \( l \) being the number of aggregated signatures and \( m \) being the number of samples.
- **norm_exposures**: The normalized exposures \( \tilde{H} \), a numeric data frame with \( l \) rows and \( m \) columns, \( l \) being the number of aggregated signatures and \( m \) being the number of samples.
- **out_sig_ind_df**: Data frame of the type signature_indices_df, i.e. indicating name, function and meta-information of the aggregated signatures.

See Also

- LCD_complex_cutoff

Examples

NULL
annotate_intermut_dist_cohort

Annotate the intermutation distance of variants cohort-wide

Description

The function annotates the intermutational distance to a cohort wide data frame by applying `annotate_intermut_dist_PID` to every PID-specific subtraction of the cohort wide data. Note that `annotate_intermut_dist_PID` calls `rainfallTransform`. If the PID information is missing, `annotate_intermut_dist_PID` is called directly for the whole input.

Usage

```r
annotate_intermut_dist_cohort(
  in_dat,
  in_CHROM.field = "CHROM",
  in_POS.field = "POS",
  in_PID.field = NULL,
  in_mode = "min",
  in_verbose = FALSE
)
```

Arguments

- **in_dat**: VRanges object, VRangesList, data frame or list of data frames which carries (at least) one column for the chromosome and one column for the position. Optionally, a column to specify the PID can be provided.
- **in_CHROM.field**: String indicating which column of `in_df` carries the chromosome information
- **in_POS.field**: String indicating which column of `in_df` carries the position information
- **in_PID.field**: String indicating which column of `in_df` carries the PID information
- **in_mode**: String passed through `annotate_intermut_dist_PID` to `rainfallTransform` indicating which method to choose for the computation of the intermutational distance.
- **in_verbose**: Whether verbose or not.

Value

VRanges object, VRangesList, data frame or list of data frames identical to `in_df` (reordered by `in_PID.field`), but with the intermutation distance annotated as an additional column on the right named `dist`.

See Also

- `annotate_intermut_dist_PID`
- `rainfallTransform`
Examples

test_df <- data.frame(CHROM=c(1,1,2,2,2,3,3,4,4,5,5),
  POS=c(1,2,4,4,6,9,1,4,8,10,20,40,100,200),
  REF=c("C","C","C","T","T","T","A",
    "A","G","G","G","N","A"),
  ALT=c("A","G","T","A","C","G","C",
    "G","T","A","C","T","A","N"),
  PID=c(1,1,1,2,2,2,1,1,2,2,2,1,1,2))

annotate_intermut_dist_PID

Annotate the intermutation distance of variants per PID

Description

The function annotates the intermutational distance to a PID wide data frame by applying `rainfallTransform` to every chromosome-specific subfraction of the PID wide data.

Usage

```r
annotate_intermut_dist_PID(
  in_dat,
  in_CHROM.field = "CHROM",
  in_POS.field = "POS",
  in_mode = "min",
  in_verbose = FALSE
)
```

Arguments

- `in_dat`: VRanges object or data frame which carries (at least) one column for the chromosome and one column for the position.
- `in_CHROM.field`: String indicating which column of `in_dat` carries the chromosome information if dealing with data frames.
- `in_POS.field`: String indicating which column of `in_dat` carries the position information if dealing with data frames.
in_mode

String passed to `rainfallTransform` indicating which method to choose for the computation of the intermutational distance.

in_verbose

Whether verbose or not.

Value

`VRanges` object or data frame identical to `in_dat`, but with the intermutation distance annotated as an additional column on the right named `dist`.

See Also

`annotate_internul_dist_cohort`
`rainfallTransform`

Examples

```r
test_df <- data.frame(CHROM=c(1,1,1,2,2,2,3,3,3,4,4,4,5,5),
                      POS=c(1,2,4,4,6,9,1,4,8,10,20,40,100,200),
                      REF=c("C","C","C","T","C","C","A","A","A","G","G","G","N","A"),
                      ALT=c("A","G","T","A","C","G","C","G","T","A","C","T","A","N"))
min_dist_df <- annotate_internul_dist_PID(test_df,in_CHROM.field="CHROM",
                                           in_POS.field="POS",
                                           in_mode="min")
max_dist_df <- annotate_internul_dist_PID(test_df,in_CHROM.field="CHROM",
                                           in_POS.field="POS",
                                           in_mode="max")
min_dist_df
max_dist_df
```

---

**annotation_exposures_barplot**

*Plot the exposures of a cohort with different layers of annotation*

**Description**

The exposures $H$, determined by NMF or by LCD, are displayed as a stacked barplot by calling `Heatmap`. The x-axis displays the PIDs (patient identifier or sample), the y-axis the counts attributed to the different signatures with their respective colours per PID. It is analogous to `plot_exposures`. As many layers of information as desired can be added via an annotation data frame. The annotation data is handled in a way similar to `annotation_heatmap_exposures`. This function calls:

- `rowAnnotation`
- `HeatmapAnnotation` and
- `Heatmap`
Usage

```
annotation_exposures_barplot(
    in_exposures_df,
    in_signatures_ind_df,
    in_subgroups_df,
    in_annotation_df = NULL,
    in_annotation_col = NULL,
    ylab = NULL,
    title = "",
    in_labels = FALSE,
    in_barplot_borders = TRUE,
    in_column_anno_borders = FALSE,
    in_annotation_legend_side = "right",
    in_padding = unit(c(2, 20, 2, 2), "mm"),
    in_annotation = NULL
)
```

Arguments

- **in_exposures_df**
  - Numerical data frame encoding the exposures, i.e., which signature contributes how much to which PID (patient identifier or sample).

- **in_signatures_ind_df**
  - A data frame containing meta information about the signatures.

- **in_subgroups_df**
  - A data frame indicating which PID (patient or sample identifier) belongs to which subgroup.

- **in_annotation_df**
  - A data frame indicating which PID (patient or sample identifier) belongs to which subgroup for all layers of annotation.

- **in_annotation_col**
  - A list indicating colour attributions for all layers of annotation.

- **ylab**
  - String indicating the column name in `in_subgroups_df` to take the subgroup information from.

- **title**
  - Title for the plot to be created.

- **in_labels**
  - Whether or not to show the names of the samples.

- **in_barplot_borders**
  - Whether or not to show border lines in barplot.

- **in_column_anno_borders**
  - Whether or not to draw separating lines between the fields in the annotation.

- **in_annotation_legend_side**
  - Where to put the legends of the annotation df, default is right.

- **in_padding**
  - Parameter passed on to function `draw`.

- **in_annotation**
  - A full annotation object may also be provided by the educated user.
Details

It might be necessary to install the newest version of the development branch of the packages circlize and ComplexHeatmap by Zuguang Gu:

```
devtools::install_github("jokergoo/circlize")
```

and

```
devtools::install_github("jokergoo/ComplexHeatmap")
```

Value

The function doesn’t return any value.

See Also

HeatmapAnnotation
Heatmap
decorate_heatmap_body
annotation_heatmap_exposures
plot_exposures

Examples

NULL

---

**annotation_exposures_list_barplot**

*Plot the exposures of a cohort with different layers of annotation for SNV and INDEL signatures*

---

Description

The exposures $H$, determined by NMF or by LCD, are displayed as a stacked barplot by calling Heatmap. The x-axis displays the PIDs (patient identifier or sample), the y-axis the counts attributed to the different signatures with their respective colours per PID. It is analogous to plot_exposures. As many layers of information as desired can be added via an annotation data frame. The annotation data is handled in a way similar to annotation_heatmap_exposures. In comparison to annotation_exposures_barplot allows this function to deal with a list of different signature and mutation types. This function calls:

- rowAnnotation,
- HeatmapAnnotation and
- Heatmap
Usage

\[
\text{annotation_exposures_list_barplot}(
\text{in_exposures_list},
\text{in_signatures_ind_list},
\text{in_subgroups_list},
\text{in_annotation_list},
\text{ylab} = \text{NULL},
\text{title} = \text{""},
\text{in_indel_sigs} = \text{FALSE},
\text{in_labels} = \text{FALSE},
\text{in_barplot_borders} = \text{TRUE},
\text{in_column_anno_borders} = \text{FALSE},
\text{in_annotation_legend_side} = \text{"right"},
\text{in_padding} = \text{unit(c(2, 20, 2, 2), \"mm\")},
\text{in_annotation} = \text{NULL}
\)
\]

Arguments

- \text{in_exposures_list}
  - A list of numerical data frame encoding the exposures \( H \) of different signature types, i.e. which signature contributes how much to which PID (patient identifier or sample).
- \text{in_signatures_ind_list}
  - A list of data frame containing meta information about each signature type individually.
- \text{in_subgroups_list}
  - A list of data frame indicating of each signature type which PID (patient or sample identifier) belongs to which subgroup.
- \text{in_annotation_list}
  - A list data frame indicating which PID (patient or sample identifier) belongs to which subgroup for all layers of annotation and a list indicating colour attributions for all layers of annotation for each signature type individually.
- \text{ylab}
  - String indicating the column name in \text{in_subgroups_df} to take the subgroup information from.
- \text{title}
  - Title for the plot to be created.
- \text{in_indel_sigs}
  - Tag which is default \text{FALSE} when whole genome data are analysed the tag will be \text{TRUE}.
- \text{in_labels}
  - Whether or not to show the names of the samples.
- \text{in_barplot_borders}
  - Whether or not to show border lines in barplot.
- \text{in_column_anno_borders}
  - Whether or not to draw separating lines between the fields in the annotation.
- \text{in_annotation_legend_side}
  - Where to put the legends of the annotation df, default is right.
- \text{in_padding}
  - Parameter passed on to function \text{draw}.
- \text{in_annotation}
  - A full annotation object may also be provided by the educated user.
Details

It might be necessary to install the newest version of the development branch of the packages circlize and ComplexHeatmap by Zuguang Gu: devtools::install_github("jokergoo/circlize") and devtools::install_github("jokergoo/ComplexHeatmap")

Value

The function doesn’t return any value.

See Also

HeatmapAnnotation
Heatmap
decorate_heatmap_body
annotation_heatmap_exposures
plot_exposures

Examples

NULL

---

annotation_heatmap_exposures

Heatmap to cluster the PIDs on their signature exposures (Complex-Heatmap)

---

Description

The PIDs are clustered according to their signature exposures. The procedure is analogous to complex_heatmap_exposures, but enabling more than one annotation row for the PIDs. This function calls:

- rowAnnotation,
- HeatmapAnnotation and
- Heatmap
Usage

annotation_heatmap_exposures(
  in_exposures_df,
  in_annotation_df,
  in_annotation_col,
  in_signatures_ind_df,
  in_data_type = "norm exposures",
  in_method = "manhattan",
  in_palette = colorRamp2(c(0, 0.2, 0.4, 0.6), c("white", "yellow", "orange", "red")),
  in_cutoff = 0,
  in_filename = NULL,
  in_column_anno_borders = FALSE,
  in_row_anno_borders = FALSE,
  in_show_PIDs = TRUE,
  in_annotation_legend_side = "right"
)

Arguments

in_exposures_df
  Numerical data frame encoding the exposures \( \mathbf{H} \), i.e. which signature contributes how much to which PID (patient identifier or sample).

in_annotation_df
  A data frame indicating which PID (patient or sample identifier) belongs to which subgroup for all layers of annotation

in_annotation_col
  A list indicating colour attributions for all layers of annotation

in_signatures_ind_df
  A data frame containing meta information about the signatures, especially the asserted colour

in_data_type
  Title in the figure

in_method
  Method of the clustering to be supplied to dist. Can be either of: euclidean, maximum, manhattan, canberra, binary or minkowski

in_palette
  Palette with colours or colour codes for the heatmap. Default is colorRamp2(c(0, 0.2, 0.4, 0.6), c("white", "yellow", "orange", "red"))

in_cutoff
  A numeric value less than 1. Signatures from within \( \mathbf{W} \) with an overall exposure less than in_cutoff will be discarded for the clustering.

in_filename
  A path to save the heatmap. If none is specified, the figure will be plotted to the running environment.

in_column_anno_borders
  Whether or not to draw separating lines between the fields in the annotation

in_row_anno_borders
  Whether or not to draw separating lines between the fields in the annotation

in_show_PIDs
  Whether or not to show the PIDs on the x-axis

in_annotation_legend_side
  Where to put the legends of the annotation df, default is right.
attribute_nucleotide_exchanges

Details

One additional parameter, in_show_legend_bool_vector, indicating which legends to display, is planned but deactivated in this version of the package. In order to use this feature, it will be necessary to install the newest version of the packages circlize and ComplexHeatmap by Zuguang Gu:

devtools::install_github("jokergoo/circlize") and devtools::install_github("jokergoo/ComplexHeatmap")

Value

The function doesn’t return any value.

See Also

Heatmap

complex_heatmap_exposures

Examples

NULL

attribute_nucleotide_exchanges

Attribute the nucleotide exchange for an SNV

Description

SNVs are grouped into 6 different categories (12/2 as reverse complements are summed over). This function defines the attribution.

Usage

attribute_nucleotide_exchanges(
  in_dat,
  in_REF.field = "REF",
  in_ALT.field = "ALT",
  inVerbose = FALSE
)

Arguments

in_dat VRanges object or data frame which carries one column for the reference base and one column for the variant base
in_REF.field String indicating which column of in_dat carries the reference base if dealing with data frames
in_ALT.field String indicating which column of in_dat carries the variant base if dealing with data frames
inVerbose Whether verbose or not.
attribute_sequence_contex_indel

**Description**

The function is a wrapper and uses `getSequenceContext` to annotate the sequence context.

**Usage**

```r
attribute_sequence_contex_indel(
  in_dat,
  in_REF.field = "REF",
  in_ALT.field = "ALT",
  in_verbose = FALSE,
  in_offsetL = 10,
  in_offsetR = 50
)
```

**Arguments**

- `in_dat`: VRanges object or data frame which carries one column for the reference base and one column for the variant base
- `in_REF.field`: String indicating which column of `in_dat` carries the reference base if dealing with data frames
- `in_ALT.field`: String indicating which column of `in_dat` carries the variant base if dealing with data frames
- `in_verbose`: Verbosity if `in_verbose`=1
- `in_offsetL`: Number of nucleotides which should be annotated downstream of the variant. Per default 10 bps are annotated
- `in_offsetR`: Number of nucleotides which should be annotated upstream of the catiant. Per default 50 bps are annotated

---

**Value**

A character vector with as many rows as there are in `in_dat` which can be annotated (i.e. appended) to the input data frame.

**Examples**

```r
test_df <- data.frame(
  CHROM=c(1,1,2,2,3,3,3,4,4,4,5,5,6,6,7,8),
  POS=c(1,2,3,4,5,6,1,2,3,4,5,6,7,8),
  REF=c("C","C","C","T","T","T","A","A","G","G","G","N","A"),
  ALT=c("A","G","T","A","C","G","C","G","T","A","C","T","A","N"))
test_df$change <- attribute_nucleotide_exchanges(
  test_df,in_REF.field = "REF",in_ALT.field = "ALT")
test_df
```
**attribution_of_indels**

**Value**

VRanges object or data frame with the same number rows and additional columns containing the type of INDEL (Ins = insertion and Del = deletion), the annotated sequence context of the defined length, the absolute number of exchanged nucleotides and the nucleotide exchange between \texttt{in\_REF.field} and \texttt{in\_ALT.field}.

**Examples**

```r
data(GenomeOfNl\_raw)
GenomeOfNl\_context <- \texttt{attribute\_sequence\_context\_indel}(
  \texttt{in\_dat} = head(GenomeOfNl\_raw),
  \texttt{in\_REF.field} = \texttt{"REF"},
  \texttt{in\_ALT.field} = \texttt{"ALT"},
  \texttt{in\_verbose} = \texttt{FALSE},
  \texttt{in\_offsetL} = 10, \texttt{in\_offsetR} = 50)
GenomeOfNl\_context
```

**Description**

Each variant is categorized into one of the 83 INDEL categories. The classification likewise to Alexandrov et al., 2018 (https://www.synapse.org/#!Synapse:syn11726616). The number of 83 features are classified as followed:

1. Deletion of 1 bp C/(G) or T/(A) in a repetitive context. The context is classified into 1, 2, 3, 4, 5 or larger or equal to 6 times the same nucleotide(s).
2. Insertion of 1 bp C/(G) or T/(A) in a repetitive context. The context is classified into 0, 1, 2, 3, 4, or larger or equal to 5 times the same nucleotide(s).
3. Deletions of 2bps, 3bps, 4bps or more or equal to 5bps in a repetitive context. Each deletion is classified in a context of 1, 2, 3, 4, 5 or larger or equal to 6 times the same motif.
4. Insertion of 2 bps, 3 bps, 4 bps or more or equal to 5 bps in a repetitive context. Each deletion is classified in a context of 0, 1, 2, 3, 4 or larger or equal to 5 times the same motif.
5. Microhomology deletion of 2bps, 3bps, 4bps or more or equal to 5 bps in a partly repetitive context. The partly repetitive context is defined by motif length of minus 1 bp, 2 bps, 3 bps, 4 bps or more or equal to 5bps, which is located before and after the break-point junction of the deletion.

**Usage**

```r
\texttt{attribution\_of\_indels(in\_dat\_return} = \texttt{in\_dat\_return})
```
The first columns are those of a standard vcf file, followed by an arbitrary number of custom or defined columns. One of these can carry a PID (patient or sample identifier) and subgroup information. Furthermore, the columns containing the sequence context and the absolute length of the INDEL as well as the INDEL type of the variant can be annotated to the vcf-like df with `attribute_sequence_context_indel`. These columns are required to enable the construction of a mutational catalog.

Value

Data frame with the same dimension as the input data frame plus an additional column with the INDEL classification number corresponding to Alexandrov et al. 2018.

Examples

```r
data(GenomeOfNl_raw)
GenomeOfNl_context <- attribute_sequence_context_indel(in_dat = head(GenomeOfNl_raw))
GenomeOfNl_classified <- attribution_of_indels(GenomeOfNl_context)
GenomeOfNl_classified
```

---

### build_gene_list_for_pathway

**Build a gene list for a given pathway name**

**Description**

Build a gene list for a given pathway name

**Usage**

```r
build_gene_list_for_pathway(in_string, in_organism)
```

**Arguments**

- `in_string`: Name or description of the pathway
- `in_organism`: Name of the taxon to be searched in

**Value**

A character vector of gene names
classify_indels

See Also

keggLink
keggFind
extract_names_from_gene_list

Examples

species <- "hsa"
gene_lists_meta_df <- data.frame(
  name=c("BER","NHEJ","MMR"),
  explanation=c("base excision repair",
                "non homologous end joining",
                "mismatch repair"))
number_of_pathways <- dim(gene_lists_meta_df)[1]
gene_lists_list <- list()
for (i in seq_len(number_of_pathways)) {
  temp_list <-
    build_gene_list_for_pathway(gene_lists_meta_df$explanation[i],
                                species)
  gene_lists_list <- c(gene_lists_list,list(temp_list))
}
gene_lists_list

classify_indels

INDEL function V1 - not compatible with AlexandrovSignatures

Description

INDEL function V1 - not compatible with AlexandrovSignatures

Usage

classify_indels(
  in_df,
  in_ALT.field = "ALT",
  in_REF.field = "REF",
  in_breaks = c(-Inf, -10, -3, 0, 2, 9, Inf),
  in_labels = c("del3", "del2", "del1", "in1", "in2", "in3")
)

Arguments

in_df Input data frame containing the variances in a vcf-like format
in_ALT.field Column number for alternative field
in_REF.field Column number for reference field
in_breaks Handed over to function cut
in_labels Handed over to function cut
compare_exposures

**Value**

classVector, a factor vector of indel sizes

**Examples**

`NULL`

---

**compare_exposures**

*Compares alternative exposures*

**Description**

Compares exposures computed by two alternative approaches for the same cohort

**Usage**

```r
compare_exposures(in_exposures1_df, in_exposures2_df, deselect_flag = TRUE)
```

**Arguments**

- `in_exposures1_df` Numeric data frame with exposures, ideally the smaller exposure data is supplied first.
- `in_exposures2_df` Numeric data frame with exposures, ideally the bigger exposure data is supplied second.
- `deselect_flag` Whether signatures absent in both exposure data frames should be removed.

**Value**

A list with entries `merge_df, all_cor.coeff, all_p.value, cor.coeff_vector, p.value_vector, all_cor.test, and cor.test_list`.

- `merge_df`: Merged molten input exposure data frames
- `all_cor.coeff`: Pearson correlation coefficient for all data points, i.e. taken all signatures together
- `all_p.value`: P-value of the Pearson test for all data points, i.e. taken all signatures together
- `cor.coeff_vector`: A vector of Pearson correlation coefficients evaluated for every signature independently
- `p.value_vector`: A vector of p-values of the Pearson tests evaluated for every signature independently
- `all_cor.test`: A data structure as returned by `cor.test` for all data points, i.e. taken all signatures together
- `cor.test_list`: A list of data structures as returned by `cor.test`, but evaluated for every signature independently
**Examples**

NULL

---

**compare_expousre_sets**  *Compare two sets of exposures by cosine distance*

**Description**

Compare two sets of exposures, stored in numerical data frames $H_1$ and $H_2$, by computing the row-wise cosine distance

**Usage**

```r
compare_expousre_sets(in_df_small, in_df_big, in_distance = cosineDist)
```

**Arguments**

- `in_df_small`, `in_df_big`
  
  Numerical data frames $H_1$ and $H_2$, ideally the bigger one first, both with $l$ rows and $m_1$ and $m_2$ columns, $l$ being the number of signatures and $m_1$ and $m_2$ being the respective numbers of samples or patient identifiers of $H_1$ and $H_2$

- `in_distance`
  
  A function which computes the distance measure, default is `cosineDist`

**Value**

A list with entries `distance`, `hierarchy_small` and `hierarchy_big`.

- `distance`: A numerical data frame with the cosine distances between the columns of $H_1$, indexing the rows, and $H_2$, indexing the columns

- `hierarchy_small`: A data frame carrying the information of ranked similarity between the signatures in $H_2$ with the signatures in $H_1$

- `hierarchy_big`: A data frame carrying the information of ranked similarity between the signatures in $H_1$ with the signatures in $H_2$

**See Also**

`cosineDist`

**Examples**

```r
sig_1_df <- data.frame(matrix(c(1,0,0,0,1,0,0,0,1,0),ncol=3))
names(sig_1_df) <- paste0("B",seq_len(dim(sig_1_df)[2]))
sig_2_df <- data.frame(matrix(c(1,1,0,0,0,1,0),ncol=2))
compare_expousre_sets(sig_1_df,sig_2_df)
```
compare_sets

Description

Compare two sets of signatures, stored in numerical data frames \( W_1 \) and \( W_2 \), by computing the column-wise cosine distance.

Usage

```r
compare_sets(in_df_small, in_df_big, in_distance = cosineDist)
```

Arguments

- `in_df_small, in_df_big`:
  Numerical data frames \( W_1 \) and \( W_2 \), ideally the bigger one first, both with \( n \) rows and \( l_1 \) and \( l_2 \) columns, \( n \) being the number of features and \( l_1 \) and \( l_2 \) being the respective numbers of signatures of \( W_1 \) and \( W_2 \).

- `in_distance`:
  A function which computes the distance measure, default is `cosineDist`.

Value

A list with entries `distance`, `hierarchy_small` and `hierarchy_big`.

- `distance`:
  A numerical data frame with the cosine distances between the columns of \( W_1 \), indexing the rows, and \( W_2 \), indexing the columns.

- `hierarchy_small`:
  A data frame carrying the information of ranked similarity between the signatures in \( W_2 \) with the signatures in \( W_1 \).

- `hierarchy_big`:
  A data frame carrying the information of ranked similarity between the signatures in \( W_1 \) with the signatures in \( W_2 \).

See Also

- `cosineDist`

Examples

```r
sig_1_df <- data.frame(matrix(c(1,0,0,0,1,0,0,0,1,0),ncol=3))
names(sig_1_df) <- paste0("B",seq_len(dim(sig_1_df)[2]))
sig_2_df <- data.frame(matrix(c(1,1,0,0,0,1,1),ncol=2))
compare_sets(sig_1_df,sig_2_df)
```
compare_SMCs

Compare all strata from different stratifications

Description

Compare all strata from different orthogonal stratification axes, i.e. orthogonal SMCs by cosine similarity of signature exposures. First calls

- make_strata_df, then
- plot_strata and finally
- make_comparison_matrix

Usage

```r
compare_SMCs(
  in_stratification_lists_list,
  in_signatures_ind_df,
  output_path,
  in_nrect = 5,
  in_attribute = ""
)
```

Arguments

- `in_stratification_lists_list` List of lists with entries from different (orthogonal) stratification axes or SMCs
- `in_signatures_ind_df` A data frame containing meta information about the signatures
- `output_path` Path to directory where the results, especially the figure produced by `corrplot` is going to be stored.
- `in_nrect` Number of clusters in the clustering procedure provided by `corrplot`
- `in_attribute` Additional string for the file name where the figure produced by `corrplot` is going to be stored.

Value

The comparison matrix of cosine similarities.

See Also

- `plot_strata`
- `make_comparison_matrix`

Examples

```r
NULL
```
### complex_heatmap_exposures

**Description**

The PIDs are clustered according to their signature exposures. uses package **ComplexHeatmap** by Zuguang Gu. This function calls:

- `rowAnnotation`
- `HeatmapAnnotation` and
- `Heatmap`

---

### compare_to_catalogues

*Compare one mutational catalogue to reference mutational catalogues*

**Description**

Compare one mutational catalogue (e.g. of one index patient) to a list of reference mutational catalogues (e.g. from the initial Alexandrov publication) by cosine similarities

**Usage**

```r
compare_to_catalogues(in_index_df, in_comparison_list)
```

**Arguments**

- `in_index_df`: Data frame containing the mutational catalogue of interest
- `in_comparison_list`: List of data frames (ideally named) containing the reference mutational catalogues

**Value**

A similarity dataframe

**Examples**

```r
NULL
```
Usage

complex_heatmap_exposures(
    in_exposures_df,
    in_subgroups_df,
    in_signatures_ind_df,
    in_data_type = "norm exposures",
    in_method = "manhattan",
    in_subgroup_column = "subgroup",
    in_subgroup_colour_column = NULL,
    in_palette = colorRamp2(c(0, 0.2, 0.4, 0.6), c("white", "yellow", "orange", "red")),
    in_cutoff = 0,
    in_filename = NULL,
    in_column_anno_borders = FALSE,
    in_row_anno_borders = FALSE
)

Arguments

in_exposures_df
    Numerical data frame encoding the exposures H, i.e. which signature contributes how much to which PID (patient identifier or sample).

in_subgroups_df
    A data frame indicating which PID (patient or sample identifier) belongs to which subgroup

in_signatures_ind_df
    A data frame containing meta information about the signatures, especially the asserted colour

in_data_type
    Title in the figure

in_method
    Method of the clustering to be supplied to dist. Can be either of: euclidean, maximum, manhattan, canberra, binary or minkowski

in_subgroup_column
    Indicates the name of the column in which the subgroup information is encoded in in_subgroups_df

in_subgroup_colour_column
    Indicates the name of the column in which the colour information for subgroups is encoded in in_subgroups_df. If NULL, a rainbow palette is used instead.

in_palette
    Palette with colours for the heatmap. Default is colorRamp2(c(0, 0.2, 0.4, 0.6), c('white', 'yellow', 'orange', 'red'))

in_cutoff
    A numeric value less than 1. Signatures from within W with an overall exposure less than in_cutoff will be discarded for the clustering.

in_filename
    A path to save the heatmap. If none is specified, the figure will be plotted to the running environment.

in_column_anno_borders
    Whether or not to draw separating lines between the fields in the annotation

in_row_anno_borders
    Whether or not to draw separating lines between the fields in the annotation
computeLogLik

Details
It might be necessary to install the newest version of the development branch of the packages circlize and ComplexHeatmap by Zuguang Gu: devtools::install_github("jokergoo/circlize")
and devtools::install_github("jokergoo/ComplexHeatmap")

Value
The function doesn’t return any value.

See Also
Heatmap

Examples

data(lymphoma_cohort_LCD_results)
complex_heatmap_exposures(
    rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df,
    COSMIC_subgroups_df,
    chosen_signatures_indices_df,
    in_data_type="norm exposures",
    in_subgroup_colour_column="col",
    in_method="manhattan",
    in_subgroup_column="subgroup")

computeLogLik compute the loglikelihood

Description
Compute the loglikelihood

Usage
computeLogLik(in_vector, in_pdf = NULL, verbose = FALSE)

Arguments

  in_vector Numeric vector of input values of which the loglikelihood is computed.
  in_pdf    Probability distribution function, if NULL a normal distribution is used.
  verbose   Verbose if in_verbose=1

Value
A numeric value (sum of the logarithms of the likelihoods of the input vector)
compute_comparison_stat_df

Extract statistical measures for entity comparison

Description

Compare one mutational catalogue (e.g. of one index patient) to a list of reference mutational catalogues (e.g. from the initial Alexandrov publication) by cosine similarities.

Usage

compute_comparison_stat_df(in_sim_df)

Arguments

in_sim_df A similarity data frame as extracted by compare_to_catalogues

Value

A dataframe containing statistical measures, prepared for bar plot.

Examples

NULL

compute_comparison_stat_df

Description

Wrapper function around confIntExp, which is applied to every signature or sample pair in a cohort. The extracted lower bound of the confidence intervals are added to the input data which is reordered and melted in order to prepare for visualization with ggplot2. The calculation of confidence intervals is based on a profiling likelihood algorithm and the wrapper calculates the data for the exposure contribution identified with SNV and INDEL signature decompositions and application of the following cutoffs:

1. CosmicValid_absCutoffVector
2. CosmicValid_normCutoffVector
3. CosmicArtif_absCutoffVector
4. CosmicArtif_normCutoffVector
5. PCAWGValidSNV_absCutoffVector
6. PCAWGValidID_absCutoffVector

The function makes use of different YAPSA functions. For each of the above stated cutoff vectors a per PID decomposition of the SNV and INDEL catalog is calculated respectively using `LCD_complex_cutoff_perPID`. In a next step, `variateExp` which is a wrapper around `confIntExp` to compute confidence intervals for a cohort is used. A dataframe is returned with the upper and lower bounds of the confidence intervals. In a last step `plotExposuresConfidence_indel` to plot the exposures to extracted signatures including confidence intervals computed with e.g. by `variateExp`.

Usage

```r
confidence_indel_only_calulation(in_current_indel_df, in_current_snv_df)
```

Arguments

- `in_current_indel_df`
  A INDEL mutational catalog. Mutational catalog can be constructed with `create_indel_mutation_catalogue_from_df`.
- `in_current_snv_df`
  A SNV mutational catalog. Mutational catalog can be constructed with `create_mutation_catalogue_from_df`.

Value

A list is returned containing 12 objects. For each cutoff data frame two corresponding object are present. First, the p table object which can be used for graphically visualization, and second a dataframe containing the corresponding upper and lower bounds of the confidence intervals.

Examples

```r
data("GenomeOfNl_MutCat")
```

---

**confidence_indel_only_calulation**

*Wrapper to compute confidence intervals for only INDEL signatures.*

Description

Wrapper function around `confIntExp`, which is applies to every signature or sample pair in a cohort. The extracted lower bound of the confidence intervals are added to the input data which is reordered and melted in order to prepare for visualization with `ggplot2`. The calculates of confidence intervals is based on a profiling likelihood algorithm and the wrapper calculates the data for the exposure contribution identified with INDEL signature decomposition and the usage of PCAWGValidID_absCutoffVector data frame.
Usage

confidence_indel_only_calulation(in_current_indel_df)

Arguments

in_current_indel_df
A INDEL mutational catalog. Mutational catalog can be constructed with create_indel_mutation_catalogue_from_df.

Details

The function makes use of different YAPSA functions. For each of the above stated cutoff vectors a per PID decomposition of the SNV and INDEL catalog is calculated respectively using LCD_complex_cutoff_perPID. In a next step, variateExp which is a wrapper around confIntExp to compute confidence intervals for a cohort is used. A dataframe is returned with the upper and lower bounds of the confidence intervals. In a last step plotExposuresConfidence_indel to plot the exposures to extracted signatures including confidence intervals computed with e.g. by variateExp.

Value

A list is returned containing two objects. First, the p gtable object which can be used for graphically visualization, and second a dataframe containing the corresponding upper and lower bounds of the confidence intervals.

Examples

data("GenomeOfNl_MutCat")
temp_list <- confidence_indel_only_calulation(  
in_current_indel_df=MutCat_indel_df)
plot(temp_list$p_complete_PCAWG_ID)
head(temp_list$complete_PCAWG_ID)

confIntExp

Compute confidence intervals

Description

Compute confidence intervals using the (log-)likelihood ratio test, primarily for one input sample.

Usage

confIntExp(  
  in_ind = 1,  
  in_sigLevel = 0.05,  
  in_delta = 1,  
  in_exposure_vector = NULL,  
  in_verbose = FALSE,  
  ...  
)
Arguments

in_ind      Index of the input signature to be variated.
in_sigLevel Significance level (one-sided)
in_delta    Inflation parameter for the alternative model.
in_exposure_vector    Exposure vector computed for the input sample.
in_verbose  Whether to run verbose (TRUE) or not (FALSE)
...

Input parameters passed on to variateExpSingle.

Value

A list with entries

- upper: Upper bound of the confidence interval
- lower: Lower bound of the confidence interval

Examples

library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
data(sigs)
word_length <- 3
temp_list <- create_mutation_catalogue_from_df(
  lymphoma_test_df,this_seqnames.field = "CHROM",
  this_start.field = "POS",this_end.field = "POS",
  this_PID.field = "PID",this_subgroup.field = "SUBGROUP",
  this_refGenome = BSgenome.Hsapiens.UCSC.hg19,
  this_wordLength = word_length)
lymphoma_catalogue_df <- temp_list$matrix
lymphoma_PIDs <- colnames(lymphoma_catalogue_df)
data("lymphoma_cohort_LCD_results")
lymphoma_exposures_df <-
  lymphoma_Nature2013_COSMIC_cutoff_exposures_df[, lymphoma_PIDs]
lymphoma_sigs <- rownames(lymphoma_exposures_df)
lymphoma_sig_df <- AlexCosmicValid_sig_df[, lymphoma_sigs]
confIntExp(in_ind = 1, in_sigLevel = 0.05, in_delta = 0.4,
in_exposure_vector = lymphoma_exposures_df[, 1],
in_catalogue_vector = lymphoma_catalogue_df[, 1],
in_sig_df = lymphoma_sig_df)
correct_rounded

Readjust the vector to its original norm after rounding

**Description**

After use of the function `round_precision` the norm of the input vector may have been altered by the rounding procedure. This function restores the norm by altering only the largest entry in the rounded vector (in order to create the least possible relative error).

**Usage**

```r
correct_rounded(x, in_interval = c(0, 1))
```

**Arguments**

- `x` vector to be rounded
- `in_interval` Interval

**Value**

The adapted form of the input vector `x`.

**Examples**

```r
NULL
```

cosineDist

Compute the cosine distance of two vectors

**Description**

Compute the cosine distance of two vectors

**Usage**

```r
cosineDist(a, b)
```

**Arguments**

- `a, b` Numerical vectors of same length

**Value**

The scalar product of the two input vectors divided by the product of the norms of the two input vectors.
Examples

```r
## 1. Orthogonal vectors:
cosineMatchDist(c(1,0),c(0,1))
## 2. Non-orthogonal vectors:
cosineMatchDist(c(1,0),c(1,1))
## Compare trigonometry:
1-cos(pi/4)
```

**cosineMatchDist**

*Compute an altered cosine distance of two vectors*

**Description**

This is an altered cosine distance: it first reduced the dimension of the two input vectors to only those coordinates where both have non-zero entries. The cosine similarity is then computed on these reduced vectors, i.e. on a sub-vector space.

**Usage**

```r
cosineMatchDist(a, b)
```

**Arguments**

- `a, b` Numerical vectors of same length

**Value**

The scalar product of the reduced input vectors divided by the product of the norms of the two reduced input vectors

**Examples**

```r
## 1. Orthogonal vectors:
cosineMatchDist(c(1,0),c(0,1))
## 2. Non-orthogonal vectors:
cosineMatchDist(c(1,0),c(1,1))
```
create_indel_mutation_catalogue_from_df

Wrapper to create an INDEL mutational catalog from a vlf-like data frame

Description

From data frame constructed from a vcf-file file the function create_indel_mutation_catalogue_from_df creates a mutational catalog V by sequentially applying the attribute_sequence_contex_indel, attribute_sequence_contex_indel and then attribution_of_indels. The runtime of the function is about 1 sec per 6 variants as sequence context as well as INDEL classification are timeconsuming to compute (optimization ongoing)

Usage

create_indel_mutation_catalogue_from_df(
  in_dat,
  in_signature_df,
  in_REF.field = "REF",
  in_ALT.field = "ALT",
  in_verbose = FALSE
)

Arguments

in_dat          A data frame constructed from a vcf-like file of a whole cohort or single-sample. The first columns are those of a standard vcf file (CHROM, POS, REF and ALT), followed by an arbitrary number of custom or used defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.

in_signature_df A numeric data frame W with n rows and l columns, n being the number of features and l being the number od signatures. Data frame containing INDEL signatures which should be used to create the mutational cataologe V.

in_REF.field    String indicating which column of in_dat carries the reference base if dealing with data frames

in_ALT.field    String indicating which column of in_dat carries the variant base if dealing with data frames

in_verbose      Verbose if in_verbose=1

Value

A dataframe in the format of a mutational catalog V, which can be used for LCD analysis
create_indel_mut_cat_from_df

Create a Mutational catalog from a data frame

Description

This function creates a mutational catalog from a data frame. It requires the returned data frame optained with `attribution_of_indels`.

Usage

```r
create_indel_mut_cat_from_df(in_df, in_signatures_df)
```

Arguments

- `in_df` A data frame constructed from a vcf-like file of a whole cohort or single-sample. The first columns are those of a standard vcf file, followed by an arbitrary number of customs or used defined columns. One if these can carry a PID (patient or sample identefyier) and the subgroup information. Additionally to construct the mutational catalog each variant needs to be characterize into one of the 83 INDEL feature classes, which can be performed with `attribution_of_indels`

- `in_signatures_df` A numeric data frame \(W\) with \(n\) rows and \(l\) columns, \(n\) being the number of features and \(l\) being the number of signatures. Data frame containing INDEL signatures which should be used to create the mutational catalog \(V\).

Value

A count dataframe, the mutational catalog \(V\) with rownames indicating the INDELs and colnames having the PIDs.
create_mutation_catalogue_from_df from df

Create a Mutational Catalogue from a data frame

Description

This function creates a mutational catalogue from a data frame. It is a wrapper function for create_mutation_catalogue_from_VR: it first creates a VRanges object from the data frame by makeVRangesFromDataFrame and then passes this object on to the above mentioned custom function.

Usage

create_mutation_catalogue_from_df(
  this_df,
  this_refGenome_Seqinfo = NULL,
  this_seqnames.field = "X.CHROM",
  this_start.field = "POS",
  this_end.field = "POS",
  this_PID.field = "PID",
  this_subgroup.field = "subgroup",
  this_refGenome,
  this_wordLength,
  thisVerbose = 1,
  this_rownames = c(),
  this_adapt_rownames = 1
)

Arguments

this_df A data frame constructed from a vcf-like file of a whole cohort. The first columns are those of a standard vcf file, followed by an arbitrary number of custom or used defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.

this_refGenome_Seqinfo A seqInfo object, referring to the reference genome used. Argument passed on to makeGRangesFromDataFrame and thus indirectly to makeGRangesFromDataFrame.
this_seqnames.field
Indicates the name of the column in which the chromosome is encoded
this_start.field
Indicates the name of the column in which the start coordinate is encoded
this_end.field
Indicates the name of the column in which the end coordinate is encoded
this_PID.field
Indicates the name of the column in which the PID (patient or sample identifier) is encoded
this_subgroup.field
Indicates the name of the column in which the subgroup information is encoded
this_refGenome
The reference genome handed over to create_mutation_catalogue_from_VR and indirectly to mutationContext and used to extract the motif context of the variants in in_vr.
this_wordLength
The size of the motifs to be extracted by mutationContext
this_verbose
Verbose if this_verbose=1
this_rownames
Optional parameter to specify rownames of the mutational catalogue V i.e. the names of the features.
this_adapt_rownames
Rownames of the output matrix will be adapted if this_adapt_rownames=1

Value
A list with entries matrix and frame obtained from create_mutation_catalogue_from_VR:

• matrix: The mutational catalogue V
• frame: Additional and meta information on rownames (features), colnames (PIDs) and subgroup attribution.

See Also
makeVRangesFromDataFrame
create_mutation_catalogue_from_VR

Examples
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
word_length <- 3
temp_list <- create_mutation_catalogue_from_df(
  lymphoma_test_df,this_seqnames.field = "CHROM",
  this_start.field = "POS",this_end.field = "POS",
  this_PID.field = "PID",this_subgroup.field = "SUBGROUP",
  this_refGenome = BSgenome.Hsapiens.UCSC.hg19,
  this_wordLength = word_length)
dim(temp_list$matrix)
head(temp_list$matrix)
create_mutation_catalogue_from_VR

Create a Mutational Catalogue from a VRanges Object

Description

This function creates a mutational catalogue from a VRanges Object by first calling `mutationContext` to establish the motif context of the variants in the input VRanges and then calling `motifMatrix` to build the mutational catalogue V.

Usage

```r
create_mutation_catalogue_from_VR(
  in_vr,
  in_refGenome,
  in_wordLength,
  in_PID.field = "PID",
  in_verbose = 0,
  in_rownames = c(),
  adapt_rownames = 1
)
```

Arguments

- `in_vr`: A VRanges object constructed from a vcf-like file of a whole cohort. The first columns are those of a standard vcf file, followed by an arbitrary number of custom or used defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.
- `in_refGenome`: The reference genome handed over to `mutationContext` and used to extract the motif context of the variants in `in_vr`.
- `in_wordLength`: The size of the motifs to be extracted by `mutationContext`.
- `in_PID.field`: Indicates the name of the column in which the PID (patient or sample identifier) is encoded.
- `in_verbose`: Verbose if `in_verbose=1`.
- `in_rownames`: Optional parameter to specify rownames of the mutational catalogue V i.e. the names of the features.
- `adapt_rownames`: Rownames of the output matrix will be adapted if `adapt_rownames=1`.

Value

A list with entries matrix, frame,
- `matrix`: The mutational catalogue V
- `frame`: Additional and meta information on rownames (features), colnames (PIIDs) and subgroup attribution.
cutoffs

See Also

mutationContext

motifMatrix

Examples

```r
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(sigs)
word_length <- 3
temp_vr <- makeVRangesFromDataFrame(
  lymphoma_test_df, in_seqnames.field="CHROM",
  in_subgroup.field="SUBGROUP", verbose_flag=1)
temp_list <- create_mutation_catalogue_from_VR(
  temp_vr, in_refGenome=BSgenome.Hsapiens.UCSC.hg19,
  in_wordLength=word_length, in_PID.field="PID",
  in_verbose=1)
dim(temp_list$matrix)
head(temp_list$matrix)
test_list <- split(lymphoma_test_df, f=lymphoma_test_df$PID)
other_list <- list()
for(i in seq_len(length(test_list))){
  other_list[[i]] <- test_list[[i]][c(1:80),]
}
other_df <- do.call(rbind, other_list)
other_vr <- makeVRangesFromDataFrame(
  other_df, in_seqnames.field="CHROM",
  in_subgroup.field="SUBGROUP", verbose_flag=1)
other_list <- create_mutation_catalogue_from_VR(
  other_vr, in_refGenome=BSgenome.Hsapiens.UCSC.hg19,
  in_wordLength=word_length, in_PID.field="PID",
  in_verbose=1, in_rownames=rownames(AlexCosmicValid_sig_df))
dim(other_list$matrix)
head(other_list$matrix)
```

cutoffs

Cutoffs for a supervised analysis of mutational signatures.

Description

Series of data frames with signature-specific cutoffs. All values represent optimal cutoffs. The optimal cutoffs were determined for different choices of parameters in the cost function of the optimization. The row index is equivalent to the ratio between costs for false negative attribution and false positive attribution. The columns correspond to the different signatures. To be used with `LCD_complex_cutoff`. There are two different sets of cutoffs one for the signatures described by Alexandrov et al. (Nature 2013) and one for the signatures documented in Alexandriv et al. (biorxiv 2018). The calculation of the PCAWG signature specific cutoffs was performed in a single-sample resolution which are both valid for whole genome and whole exome sequencing data analysis.
cutoffCosmicValid_rel_df: Optimal cutoffs for AlexCosmicValid_sig_df, i.e. COSMIC signatures, only validated, trained on relative exposures.

cutoffCosmicArtif_rel_df: Optimal cutoffs for AlexCosmicArtif_sig_df, i.e. COSMIC signatures, including artifact signatures, trained on relative exposures.

cutoffCosmicValid_abs_df: Optimal cutoffs for AlexCosmicValid_sig_df, i.e. COSMIC signatures, only validated, trained on absolute exposures.

cutoffCosmicArtif_abs_df: Optimal cutoffs for AlexCosmicArtif_sig_df, i.e. COSMIC signatures, including artifact signatures, trained on absolute exposures.

cutoffInitialValid_rel_df: Optimal cutoffs for AlexInitialValid_sig_df, i.e. initially published signatures, only validated signatures, trained on relative exposures.

cutoffInitialArtif_rel_df: Optimal cutoffs for AlexInitialArtif_sig_df, i.e. initially published signatures, including artifact signatures, trained on relative exposures.

cutoffInitialValid_abs_df: Optimal cutoffs for AlexInitialValid_sig_df, i.e. initially published signatures, only validated signatures, trained on absolute exposures.

cutoffInitialArtif_abs_df: Optimal cutoffs for AlexInitialArtif_sig_df, i.e. initially published signatures, including artifact signatures, trained on absolute exposures.

Usage

data(cutoffs)

Author(s)

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

---

cutoffs_pcawg

Opt. cutoffs, PCAWG SNV signatures, including artifacts

Description

cutoffPCAWG_SBS_WGSWES_artifPid_df: Optimal cutoffs for PCAWG_SP_SBS_sigs_Artif_df, i.e. initially published signatures, including artifact signatures, trained in a single-sample resolution.

cutoffPCAWG_SBS_WGSWES_realPid_df: Optimal cutoffs for PCAWG_SP_SBS_sigs_Real_df, i.e. initially published signatures, only validated signatures, trained in a single-sample resolution.

cutoffPCAWG_ID_WGS_Pid_df: Optimal cutoffs for PCAWG_SP_ID_sigs_df, i.e. initially published signatures, signatures, trained in a single-sample resolution.

Usage

data(cutoffs_pcawg)

Author(s)

Lea Jopp-Saile <huebschmann.daniel@goolemail.com>
**cut_breaks_as_intervals**

*Wrapper for cut*

**Description**

In this wrapper function for the known `cut` function, the breaks vector need not be supplied directly, instead, for every break, an interval is supplied and the function optimizes the choice of the breakpoint by choosing a local minimum of the distribution.

**Usage**

```r
cut_breaks_as_intervals(
  in_vector,
  in_outlier_cutoffs = c(0, 3000),
  in_cutoff_ranges_list = list(c(60, 69), c(25, 32)),
  in_labels = c("late", "intermediate", "early"),
  in_name = "",
  output_path = NULL
)
```

**Arguments**

- `in_vector` Vector of numerical continuously distributed input
- `in_outlier_cutoffs` Interval specifying the upper and lower bounds of the range to be considered
- `in_cutoff_ranges_list` List of intervals in which the cutoffs for `cut` have to be optimized.
- `in_labels` Labels assigned to the strata or factors returned
- `in_name` String specifying the name of the quantity analyzed (and plotted on the x-axis of the figure to be created).
- `output_path` Path where the figure produced by the density function should be stored if non-NULL.

**Value**

A list with entries `category_vector`, `density_plot` and `cutoffs`

- `category_vector`: Factor vector of the categories or strata, of the same length as `in_vector`
- `density_plot`: Density plot produced by the density function and indication of the chosen cutoffs.
- `cutoffs`: Vector of the computed optimal cutoffs

**See Also**

- `cut`
- `density`
**Examples**

```r
data(lymphoma_test)
lymphoma_test_df$random_norm <- rnorm(dim(lymphoma_test_df)[1])
temp_list <- cut_breaks_as_intervals(
  lymphoma_test_df$random_norm,
  in_outlier_cutoffs=c(-4,4),
  in_cutoff_ranges_list=list(c(-2.5,-1.5),c(0.5,1.5)),
  in_labels=c("small","intermediate","big"))
temp_list$density_plot
```

---

**deriveSigInd_df**  
*Derive a signature_indices_df object*

**Description**

Derive a data frame of type signature_indices_df (additional information for a set of signatures) from a set of given signatures for a set of new signatures.

**Usage**

```
deriveSigInd_df(querySigs, subjectSigs, querySigInd = NULL, in_sort = FALSE)
```

**Arguments**

- **querySigs**  
The signatures to compare to (given signatures).
- **subjectSigs**  
The signatures to be compared (new signatures). Alternatively this may be a complex object of type list and contain data from different deconvolutions, each of which having a set of signatures to be compared.
- **querySigInd**  
The object of type signature_indices_df (additional information for a set of signatures) belonging to the set of known signatures.
- **in_sort**  
Whether to sort or not

**Value**

An object of type signature_indices_df (additional information for a set of signatures) belonging to the set of new signatures.

**See Also**

- `relateSigs`

**Examples**

NULL
disambiguateVector  Disambiguate a vector

**Description**
Add numbered suffixes to redundant entries in a vector

**Usage**

```r
disambiguateVector(in_vector)
```

**Arguments**

- `in_vector` Input vector

**Value**
The disambiguated vector.

**Examples**

NULL

enrichSigs  Compare to background distribution

**Description**
Compare exposures from an analysis of mutational signatures in a cohort of interest to exposures computed in a background (e.g. the set of WES and WGS samples from Alexandrov 2013).

**Usage**

```r
enrichSigs(in_cohort_exposures_df, in_background_exposures_df, in_sig_df)
```

**Arguments**

- `in_cohort_exposures_df` Numerical data frame of the exposures of the cohort of interest.
- `in_background_exposures_df` Numerical data frame of the exposures of the background.
- `in_sig_df` Numerical data frame encoding the mutational signatures.

**Value**
A data frame with counts and p-values from Fisher tests.
Examples

NULL

---

**ExampleINDEL_YAPSA**

*Data structures used in examples, Indel tests and the Indel signature vignette of the YAPSA package.*

---

**Description**

Data structures used in examples, Indel tests and the Indel signature vignette of the YAPSA package.

**Author(s)**

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

**References**


---

**ExampleYAPSA**

*Test and example data*

---

**Description**

Data structures used in examples, SNV tests and the SNV signature vignette of the YAPSA package.

**lymphoma_PID_df**

A data frame carrying subgroup information for a subcohort of samples used in the vignette. Data in the vignette is downloaded from ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt. In the file available under that link somatic point mutation calls from several samples are listed in a vcf-like format. One column encodes the sample the variant was found in. In the vignette we want to restrict the analysis to only a fraction of these involved samples. The data frame `lymphoma_PID_df` carries the sample identifiers (PID) as rownames and the attributed subgroup in a column called `subgroup`.

**lymphoma_test_df**

A data frame carrying point mutation calls. It represents a subset of the data stored in ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt. In the file available under that link somatic point mutation calls from several samples are listed in a vcf-like format. One column encodes the sample the variant was found in. The data frame `lymphoma_test_df` has only the variants occurring in the sample identifiers (PIDs) 4112512, 4194218 and 4121361.

**lymphoma_Nature2013_raw_df**

A data frame carrying point mutation calls. It represents a subset of the data stored in ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt. In the file available under that link somatic point mutation calls from several samples are listed in a vcf-like format. One column encodes the sample the variant was found in. The data frame `lymphoma_Nature2013_raw_df` has only the variants occurring in the sample identifiers (PIDs) 4112512, 4194218 and 4121361.
In the file available under that link somatic point mutation calls from several samples are listed in a vcf-like format. One column encodes the sample the variant was found in.


**COSMIC_subgroups_df**: Subgroup information for the data stored in lymphoma_Nature2013_COSMIC_cutoff_exposures_df and rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df.

**chosen_AlexInitialArtif_sigInd_df**: Signature information for the data stored in lymphoma_Nature2013_COSMIC_cutoff_exposures_df and rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df.

**chosen_signatures_indices_df**: Signature information for the data stored in lymphoma_Nature2013_COSMIC_cutoff_exposures_df and rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df.

### Usage

```r
data(lymphoma_PID)
data(lymphoma_test)
data(lymphoma_Nature2013_raw)
data(lymphoma_cohort_LCD_results)
data(lymphoma_cohort_LCD_results)
data(lymphoma_cohort_LCD_results)
data(lymphoma_cohort_LCD_results)
data(lymphoma_cohort_LCD_results)
data(lymphoma_cohort_LCD_results)
```

### Author(s)

Daniel Huebschmann <huebschmann.daniel@gmail.com>

### References


### Examples

```r
data(lymphoma_test)
head(lymphoma_test_df)
dim(lymphoma_test_df)
```
**exchange_colour_vector**

*Colours codes for displaying SNVs*

**Description**

Vector attributing colours to nucleotide exchanges used when displaying SNV information, e.g. in a rainfall plot.

**Usage**

data(exchange_colour_vector)

**Value**

A named character vector

**Author(s)**

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

---

**exome_mutCatRaw_df**  
*Example mutational catalog for the exome vignette*

**Description**

`exome_mutCatRaw_df`: A data frame in the format of a SNV mutation catalog. The mutational catalog contains SNV variants from a cohort of small-cell lung cancer published by Rudin et al. (Nature Genetics 2012) which was later used in the de novo discovery analysis of mutational signatures in human cancer by Alexandrov et al. (Nature 2013).

**Usage**

data(smallCellLungCancerMutCat_NatureGenetics2012)

**Value**

A data frame in the layout of a SNV mutational catalog
References

https://www.nature.com/articles/ng.2405

Examples

```r
data(smallCellLungCancerMutCat_NatureGenetics2012)
head(exome_mutCatRaw_df)
dim(exome_mutCatRaw_df)
```

---

```r
exposures_barplot

Wrapper for enhanced_barplot

Description

Wrapper for enhanced_barplot

Usage

```r
exposures_barplot(
  in_exposures_df,
  in_signatures_ind_df = NULL,
  in_subgroups_df = NULL,
  in_sum_ind = NULL,
  in_subgroups.field = "subgroup",
  in_title = "",
  in_labels = TRUE,
  in_show_subgroups = TRUE,
  ylab = NULL,
  in_barplot_borders = TRUE,
  in_column_anno_borders = FALSE
)
```

Arguments

```r
in_exposures_df
  Numerical data frame encoding the exposures H, i.e. which signature contributes how much to which PID (patient identifier or sample).

in_signatures_ind_df
  A data frame containing meta information about the signatures. If NULL, the colour information for the signatures is taken from a rainbow palette.

in_subgroups_df
  A data frame indicating which PID (patient or sample identifyer) belongs to which subgroup. If NULL, it is assumed that all PIDs belong to one common subgroup. The colour coding for the default subgroup is red.

in_sum_ind
  Index vector influencing the order in which the PIDs are going to be displayed
```
in_subgroups.field
String indicating the column name in in_subgroups_df to take the subgroup information from.

in_title
Title for the plot to be created.

in_labels
Flag, if TRUE the PIDs are displayed on the x-axis

in_show_subgroups
Flag, if TRUE then PIDs are grouped by subgroups

ylab
Label of the y-axis on the plot to be generate

in_barplotBorders
Whether or not to show border lines in barplot

in_column_anno_borders
Whether or not to draw separating lines between the fields in the annotation

Value
The generated barplot - a ggplot2 plot

Examples

data(lymphoma_cohort_LCD_results)
exposures_barplot(lymphoma_Nature2013_COSMIC_cutoff_exposures_df,
chosen_signatures_indices_df,
COSMIC_subgroups_df)

extract_names_from_gene_list
Return gene names from gene lists

Description
Return gene names from gene lists

Usage
extract_names_from_gene_list(in_KEGG_gene_list, l)

Arguments
in_KEGG_gene_list
Gene list to extract names from

l
Index of the gene to be extracted

Value
The gene name.
Find samples affected by SNVs in a certain pathway

Usage

```r
find_affected_PIDs(in_gene_list, in_gene_vector, in_PID_vector)
```

Arguments

- `in_gene_list`: List of genes in the pathway of interest.
- `in_gene_vector`: Character vector for genes annotated to SNVs as in `vcf_like_df`.
- `in_PID_vector`: Character vector for sample names annotated to SNVs as in `vcf_like_df`.

Value

A character vector of the names of the affected samples

Examples

NULL
**GenomeOfNl_raw**

*Example data for the Indel vignette*

**Description**

GenomeOfNl_raw: A data frame contains the gemiline variants of the dutch population, carrying point mutation calls. It represents a subset of the data stored in ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt. In the file available under that link, somatic point mutation calls from several samples are listed in a vcf-like format. One column encodes the sample the variant was found in.

**Usage**

```r
data(GenomeOfNl_raw)
```

**Value**

A data frame in a vcf-like format

**References**

release version 5 [https://www.nlgenome.nl/menu/main/app-go-nl/?page_id=9](https://www.nlgenome.nl/menu/main/app-go-nl/?page_id=9)

**Examples**

```r
data(GenomeOfNl_raw)
head(GenomeOfNl_raw)
dim(GenomeOfNl_raw)
```

---

**getSequenceContext**

*Extracts the sequence context up and downstream of a nucleotide position*

**Description**

Extracts the sequence context up and downstream of a nucleotide position

**Usage**

```r
getSequenceContext(position, chr, offsetL = 10, offsetR = 50)
```
get_extreme_PIDs

Arguments

position    Start position of the considered INDEL
chr         Chromosome of the considered INDEL
offsetL     Number of nucleotides downstream of position
offsetR     Number of nucleotides upstream of position

Value

Returns a character string containing the defined sequence context

Examples

library(Biostrings)
library(BSgenome.Hsapiens.UCSC.hg19)

sequence_context <- getSequenceContext(position = 123456789, chr = "chr12",
                                          offsetL= 10, offsetR=50)

sequence_context

get_extreme_PIDs

Return those PIDs which have an extreme pattern for signature exposure

Description

For all signatures found in a project, this function returns the sample identifiers (PIDs) with extremely high or extremely low exposures of the respective signatures.

Usage

get_extreme_PIDs(in_exposures_df, in_quantile = 0.03)

Arguments

in_exposures_df          Data frame with the signature exposures
in_quantile             Quantile for the amount of extreme PIDs to be selected.

Value

A data frame with 4 rows per signature (high PIDs, high exposures, low PIDs, low exposures); the number of columns depends on the quantile chosen.

Examples

data(lymphoma_cohort_LCD_results)
get_extreme_PIDs(lymphoma_Nature2013_COSMIC_cutoff_exposures_df, 0.05)
hclust_exposures

Cluster the PIDs according to their signature exposures

Description

The PIDs are clustered according to their signature exposures by calling first creating a distance matrix:

- dist, then
- hclust and then
- labels_colors to colour the labels (the text) of the leaves in the dendrogram.

Typically one colour per subgroup.

Usage

hclust_exposures(
  in_exposures_df,
  in_subgroups_df,
  in_method = "manhattan",
  in_subgroup_column = "subgroup",
  in_palette = NULL,
  in_cutoff = 0,
  in_filename = NULL,
  in_shift_factor = 0.3,
  in_cex = 0.2,
  in_title = "",
  in_plot_flag = FALSE
)

Arguments

in_exposures_df Numerical data frame encoding the exposures H, i.e. which signature contributes how much to which PID (patient identifier or sample).

in_subgroups_df A data frame indicating which PID (patient or sample identifier) belongs to which subgroup.

in_method Method of the clustering to be supplied to dist. Can be either of: euclidean, maximum, manhattan, canberra, binary or minkowski.

in_subgroup_column Indicates the name of the column in which the subgroup information is encoded in in_subgroups_df.

in_palette Palette with colours or colour codes for the labels (the text) of the leaves in the dendrogram. Typically one colour per subgroup. If none is specified, a rainbow palette of the length of the number of subgroups will be used as default.
in_cutoff  A numeric value less than 1. Signatures from within W with an overall exposure less than in_cutoff will be discarded for the clustering.

in_filename  A path to save the dendrogram. If none is specified, the figure will be plotted to the running environment.

in_shift_factor  Graphical parameter to adjust figure to be created

in_cex  Graphical parameter to adjust figure to be created

in_title  Title in the figure to be created under in_filename

in_plot_flag  Whether or not to display the dendrogram

Value

A list with entries hclust and dendrogram.

- hclust: The object created by hclust
- dendrogram: The above object wrapped in as.dendrogram

See Also

hclust
dist
labels_colors

Examples

data(lymphoma_cohort_LCD_results)
hclust_exposures(rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df,
COSMIC_subgroups_df,
in_method="manhattan",
in_subgroup_column="subgroup")

Description

LCD performs a mutational signatures decomposition of a given mutational catalogue V with known signatures W by solving the minimization problem \( \min(||W \ast H - V||) \) with additional constraints of non-negativity on H where W and V are known

Usage

LCD(in_mutation_catalogue_df, in_signatures_df, in_per_sample_cutoff = 0)
**Arguments**

in\_mutation\_catalogue\_df

A numeric data frame V with n rows and m columns, n being the number of features and m being the number of samples

in\_signatures\_df

A numeric data frame W with n rows and l columns, n being the number of features and l being the number of signatures

in\_per\_sample\_cutoff

A numeric value less than 1. Signatures from within W with an exposure per sample less than in\_cutoff will be discarded.

**Value**

The exposures H, a numeric data frame with l rows and m columns, l being the number of signatures and m being the number of samples

**See Also**

lsei

**Examples**

```r
## define raw data
W\_prim <- matrix(c(1,2,3,4,5,6),ncol=2)
W\_prim\_df <- as.data.frame(W\_prim)
W\_df <- YAPSA:::normalize\_df\_per\_dim(W\_prim\_df,2) # corresponds to the sigs
W <- as.matrix(W\_df)
## 1. Simple case: non-negativity already in raw data
H <- matrix(c(2,5,3,6,1,9,1,2),ncol=4)
H\_df <- as.data.frame(H) # corresponds to the exposures
V <- W %*% H # matrix multiplication
V\_df <- as.data.frame(V) # corresponds to the mutational catalogue
exposures\_df <- YAPSA:::LCD(V\_df,W\_df)
## 2. more complicated: raw data already contains negative elements
## define indices where sign is going to be swapped
sign\_ind <- c(5,7)
## now compute the indices of the other fields in the columns affected
## by the sign change
row\_ind <- sign\_ind %% dim(H)[1]
temp\_ind <- 2*row\_ind -1
other\_ind <- sign\_ind + temp\_ind
## alter the matrix H to yield a new mutational catalogue
H\_compl <- H
H\_compl[sign\_ind] <- (-1)*H[sign\_ind]
H\_compl\_df <- as.data.frame(H\_compl) # corresponds to the exposures
V\_compl <- W %*% H\_compl # matrix multiplication
V\_compl\_df <- as.data.frame(V\_compl) # corresponds to the mutational catalogue
exposures\_df <- YAPSA:::LCD(V\_compl\_df,W\_df)
exposures <- as.matrix(exposures\_df)
```
LCD_complex_cutoff

**Description**

LCD_cutoff performs a mutational signatures decomposition by Linear Combination Decomposition (LCD) of a given mutational catalogue \( V \) with known signatures \( W \) by solving the minimization problem \( \min(||W \ast H - V||) \) with additional constraints of non-negativity on \( H \) where \( W \) and \( V \) are known, but excludes signatures with an overall contribution less than a given signature-specific cutoff (and thereby accounting for a background model) over the whole cohort.

LCD_complex_cutoff_perPID is a wrapper for LCD_complex_cutoff and runs individually for every PID.

LCD_extractCohort_callPerPID runs LCD_complex_cutoff and takes the identified signatures as input for LCD_complex_cutoff_perPID.

LCD_complex_cutoff_consensus calls LCD_complex_cutoff_combined AND LCD_complex_cutoff_perPID and makes a consensus signature call set.

**Usage**

```r
LCD_complex_cutoff(
    in_mutation_catalogue_df, 
    in_signatures_df, 
    in_cutoff_vector = NULL, 
    in_filename = NULL, 
    in_method = "abs", 
    in_per_sample_cutoff = 0, 
    in_rescale = TRUE, 
    in_sig_ind_df = NULL, 
    in_cat_list = NULL
)
```

```r
LCD_complex_cutoff_perPID(
    in_mutation_catalogue_df, 
    in_signatures_df, 
    in_cutoff_vector = NULL, 
    in_filename = NULL, 
    in_method = "abs", 
    in_rescale = TRUE, 
    in_sig_ind_df = NULL, 
    in_cat_list = NULL, 
    minimumNumberOfAlterations = 25
)```
LCD_extractCohort_callPerPID(
    in_mutation_catalogue_df,
    in_signatures_df,
    in_cutoff_vector = NULL,
    in_filename = NULL,
    in_method = "abs",
    in_rescale = TRUE,
    in_sig_ind_df = NULL,
    in_cat_list = NULL,
    in_verbose = FALSE,
    minimumNumberOfAlterations = 25,
    cutoff_type = "adaptive"
)

LCD_complex_cutoff_consensus(
    in_mutation_catalogue_df = NULL,
    in_signatures_df = NULL,
    in_cutoff_vector = NULL,
    in_filename = NULL,
    in_method = "abs",
    in_rescale = TRUE,
    in_sig_ind_df = NULL,
    in_cat_list = NULL,
    in_cohort_LCDlist = NULL,
    in_perPID_LCDlist = NULL,
    addSigs_cohort_cutoff = 0.25,
    addSigs_perPID_cutoff = 0.25,
    addSigs_relAbs_cutoff = 0.01,
    keep.unassigned = FALSE,
    keep.all.cohort.sigs = TRUE,
    in_verbose = FALSE,
    minimumNumberOfAlterations = 25
)

LCD_complex_cutoff_combined(
    in_mutation_catalogue_df = NULL,
    in_signatures_df = NULL,
    in_cutoff_vector = NULL,
    in_filename = NULL,
    in_method = "abs",
    in_rescale = TRUE,
    in_sig_ind_df = NULL,
    in_cat_list = NULL,
    addSigs_cohort_cutoff = 0.25,
    addSigs_perPID_cutoff = 0.25,
    addSigs_relAbs_cutoff = 0.01,
    keep.all.cohort.sigs = TRUE,
    in_verbose = FALSE,
minimumNumberOfAlterations = 25,
cutoff_type = "adaptive"
)

Arguments

in_mutation_catalogue_df
A numeric data frame $V$ with $n$ rows and $m$ columns, $n$ being the number of features and $m$ being the number of samples

in_signatures_df
A numeric data frame $W$ with $n$ rows and 1 columns, $n$ being the number of features and 1 being the number of signatures

in_cutoff_vector
A numeric vector of values less than 1. Signatures from within $W$ with an overall exposure less than the respective value in in_cutoff_vector will be discarded.

in_filename
A path to generate a histogram of the signature exposures if non-NULL

in_method
Indicate to which data the cutoff shall be applied: absolute exposures, relative exposures

in_per_sample_cutoff
A numeric value less than 1. Signatures from within $W$ with an exposure per sample less than in_cutoff will be discarded.

in_rescale
Boolean, if TRUE (default) the exposures are rescaled such that colSums over exposures match colSums over mutational catalogue

in_sig_ind_df
Data frame of type signature_indices_df, i.e. indicating name, function and meta-information of the signatures. Default is NULL.

in_cat_list
List of categories for aggregation. Have to be among the column names of in_sig_ind_df. Default is NULL.

minimumNumberOfAlterations
The perPID part of the analysis issues a warning if one sample has less mutations than this minimum cutoff.

in_verbose
Verbose if in_verbose=1

cutoff_type
If chosen to be "adaptive", the default, then signature-specific cutoffs are used for the the per-PID analysis in LCD_extractCohort_callPerPID, otherwise, no cutoffs are used.

in_cohort_LCDlist
Optional, if not provided, the cohort-wide exposures are recalculated by calling LCD_complex_cutoff

in_perPID_LCDlist
Optional, if not provided, the per sample exposures are recalculated by calling LCD_complex_cutoff_perPID

addSigs_cohort_cutoff
Numeric value for a cutoff: signatures which are detected in a fraction of the samples of the cohort greater than this cutoff are kept for the consensus set of signatures
addSigs_perPID_cutoff
Numeric value for a cutoff: signatures which are detected in one sample with exposure greater than this cutoff are kept for the consensus set of signatures

addSigs_relAbs_cutoff
Numeric value for a cutoff: signatures which are detected with at least this fraction of all variants cohort wide are kept for the consensus set of signatures

keep.unassigned
Boolean, if TRUE the exposures from the signatures which don’t fulfill the criteria to be kept will be added and stored in the exposures as "unassigned", otherwise the exposures are rescaled.

keep.all.cohort.sigs
If TRUE (default), all signatures extracted cohort wide are kept, if FALSE, the function reevaluates whether the signatures extracted cohort wide still fulfill their criteria (i.e. exposures > cutoff) after perPID extraction.

Value
A list with entries:

• exposures: The exposures $H$, a numeric data frame with $l$ rows and $m$ columns, $l$ being the number of signatures and $m$ being the number of samples

• norm_exposures: The normalized exposures $H$, a numeric data frame with $l$ rows and $m$ columns, $l$ being the number of signatures and $m$ being the number of samples

• signatures: The reduced signatures that have exposures bigger than in_cutoff

• choice: Index vector of the reduced signatures in the input signatures

• order: Order vector of the signatures by exposure

• residual_catalogue: Numerical data frame (matrix) of the difference between fit (product of signatures and exposures) and input mutational catalogue

• rss: Residual sum of squares (i.e. sum of squares of the residual catalogue)

• cosDist_fit_orig_per_matrix: Cosine distance between the fit (product of signatures and exposures) and input mutational catalogue computed after putting the matrix into vector format (i.e. one scaler product for the whole matrix)

• cosDist_fit_orig_per_col: Cosine distance between the fit (product of signatures and exposures) and input mutational catalogue computed per column (i.e. per sample, i.e. as many scaler products as there are samples in the cohort)

• sum_ind: Decreasing order of mutational loads based on the input mutational catalogue

• out_sig_ind_df: Data frame of the type signature_indices_df, i.e. indicating name, function and meta-information of the signatures. Default is NULL, non-NULL only if in_sig_ind_df is non-NULL.

• aggregate_exposures_list: List of exposure data frames aggregated over different categories. Default is NULL, non-NULL only if in_sig_ind_df and in_cat_list are non-NULL and if the categories specified in in_cat_list are among the column names of in_sig_ind_df.
See Also

LCD
aggregate_exposures_by_category
lsei

Examples

NULL

---

**LCD_SMC**  
*CD stratification analysis*

**Description**

CD stratification analysis

**Usage**

```r
LCD_SMC(in_mutation_sub_catalogue_list, in_signatures_df, in_F_df = NULL)
```

**Arguments**

- `in_mutation_sub_catalogue_list`
  A list of \(s\) stratified mutational catalogues \(\{V_i\}\) (numeric data frames) with \(n\) rows and \(m\) columns each, \(n\) being the number of features and \(m\) being the number of samples. This list is naturally provided in `run_SMC`.

- `in_signatures_df`
  A numeric data frame \(W\) with \(n\) rows and \(l\) columns, \(n\) being the number of features and \(l\) being the number of signatures

- `in_F_df`
  Default NULL

**Value**

Returns a list with all exposures and the stratified ones
logLikelihood  

Compute a loglikelihood ratio test

**Description**

Compute a likelihood ratio test based on the loglikelihoods of the residuals of two different models of the same data.

**Usage**

```r
logLikelihood(
  in_1,
  in_2,
  df_1 = NULL,
  df_2 = NULL,
  in_pdf = NULL,
  verbose = FALSE
)
```

**Arguments**

- `in_1` Residuals of model 1 of the input data.
- `in_2` Residuals of model 2 of the input data.
- `df_1` Degrees of freedom of the input model 1. If either `df_1` or `df_2` is NULL, the difference between the degrees of freedom of the two models is assumed to be 1.
- `df_2` Degrees of freedom of the input model 2. If either `df_1` or `df_2` is NULL, the difference between the degrees of freedom of the two models is assumed to be 1.
- `in_pdf` Probability distribution function, passed on to `computeLogLik`, if NULL a normal distribution is used.
- `verbose` Verbose if `in_verbose=1`

**Value**

A list with entries

- `statistic`: The test statistic
- `delta_df`: The difference in degrees of freedom between input model 1 and 2
- `p.value`: p value of the statistical test.
Examples

```r
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(sigs)
data(cutoffs)
word_length <- 3
temp_list <- create_mutation_catalogue_from_df(
  lymphoma_test_df, this_seqnames.field = "CHROM",
  this_start.field = "POS", this_end.field = "POS",
  this_PID.field = "PID", this_subgroup.field = "SUBGROUP",
  this_refGenome = BSgenome.Hsapiens.UCSC.hg19,
  this_wordLength = word_length)
lymphoma_catalogue_df <- temp_list$matrix
lymphoma_PIDs <- colnames(lymphoma_catalogue_df)
current_sig_df <- AlexCosmicValid_sig_df
current_sigInd_df <- AlexCosmicValid_sigInd_df
current_cutoff_vector <- cutoffCosmicValid_rel_df[6, ]
iniLCDList <- LCD_complex_cutoff(
  in_mutation_catalogue_df = lymphoma_catalogue_df[, 1, drop = FALSE],
  in_signatures_df = current_sig_df,
  in_cutoff_vector = current_cutoff_vector,
  in_method = "relative", in_rescale = TRUE,
  in_sig_ind_df = current_sigInd_df)
current_sig_df <- AlexCosmicValid_sig_df[, -9]
current_sigInd_df <- AlexCosmicValid_sigInd_df[-9,]
current_cutoff_vector <- cutoffCosmicValid_rel_df[6, -9]
redLCDList <- LCD_complex_cutoff(
  in_mutation_catalogue_df = lymphoma_catalogue_df[, 1, drop = FALSE],
  in_signatures_df = current_sig_df,
  in_cutoff_vector = current_cutoff_vector,
  in_method = "relative", in_rescale = TRUE,
  in_sig_ind_df = current_sigInd_df)
logLikelihood(iniLCDList, redLCDList)
```

**lymphomaNature2013_mutCat_df**

Example mutational catalog for the SNV vignette

Description

lymphomaNature2013_mutCat_df: A data frame in the format of a SNV mutation catalog. The mutational catalog contains SNV variants from the lymphoma_Nature2013_raw_df data. Mutational catalog was created with `create_mutation_catalogue_from_df` function.

Usage

```r
data(lymphomaNature2013_mutCat_df)
```
makeVRangesFromDataFrame

Value

A data frame in the layout of a SNV mutational catalog

References

ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt

Examples

data(lymphomaNature2013_mutCat_df)
head(lymphomaNature2013_mutCat_df)
dim(lymphomaNature2013_mutCat_df)

makeVRangesFromDataFrame

Construct a VRanges Object from a data frame

Description

In this package, big data frames are generated from cohort wide vcf-like files. This function constructs a VRanges object from such a data frame by using makeGRangesFromDataFrame from the package GenomicRanges

Usage

makeVRangesFromDataFrame(
  in_df,
  in_keep.extra.columns = TRUE,
  in_seqinfo = NULL,
  in_seqnames.field = "X.CHROM",
  in_start.field = "POS",
  in_end.field = "POS",
  in_PID.field = "PID",
  in_subgroup.field = "subgroup",
  in_strand.field = "strand",
  verbose_flag = 1
)

Arguments

  in_df  A big dataframe constructed from a vcf-like file of a whole cohort. The first columns are those of a standard vcf file, followed by an arbitrary number of custom or user defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.
in_keep.extra.columns

in_seqinfo Argument passed on to makeGRangesFromDataFrame

in_seqinfo A seqInfo object, referring to the reference genome used. Argument passed on to makeGRangesFromDataFrame

in_seqnames.field Indicates the name of the column in which the chromosome is encoded

in_start.field Indicates the name of the column in which the start coordinate is encoded

in_end.field Indicates the name of the column in which the end coordinate is encoded

in_PID.field Indicates the name of the column in which the PID (patient or sample identifier) is encoded

in_subgroup.field Indicates the name of the column in which the subgroup information is encoded

in_strand.field Indicates the name of the column in which the strandedness is encoded

verbose_flag Verbose if 1

Value

The constructed VRanges object

See Also

makeGRangesFromDataFrame

Examples

data(lymphoma_test)
temp_vr <- makeVRangesFromDataFrame(lymphoma_test_df,
in_seqnames.field="CHROM",
in_subgroup.field="SUBGROUP",
verbose_flag=1)

make_catalogue_strata_df

Group strata from different stratification axes

Description

For a comparison of the strata from different orthogonal stratification axes, i.e. orthogonal SMCs, the strata have to be grouped and reformatted. This function does this task for the comparison by cosine similarity of mutational catalogues. Output of this function is the basis for applying make_comparison_matrix. It is called by the wrapper function run_comparison_catalogues.
Usage

```r
make_catalogue_strata_df(
    in_stratification_lists_list,
    in_additional_stratum = NULL
)
```

Arguments

- `in_stratification_lists_list`: List of lists with entries from different (orthogonal) stratification axes or SMCs.
- `in_additional_stratum`: Include an additionally supplied stratum in comparison in non-NULL.

Value

A list with entries `strata_df`, `number_of_SMCs`, `number_of_strata`.

- `strata_df`: Pasted numerical data frame of all strata (these are going to be compared e.g. by `make_comparison_matrix`).
- `number_of_SMCs`: Number of orthogonal stratifications in `in_stratification_lists_list` and additional ones.
- `number_of_strata`: Cumulative number of strata (sum over the numbers of strata of the different stratifications in `in_stratification_lists_list`) and additional ones.

See Also

- `plot_strata`
- `make_comparison_matrix`
- `run_comparison_catalogues`

Examples

```r
NULL
```

**Description**

Compute and plot a similarity matrix for different strata from different stratification axes together. First, `compare_sets` is called on `in_strata_df` with itself, yielding a distance matrix (a numerical data frame) `dist_df` of the strata. The corresponding similarity matrix `1-dif_df` is then passed to `corrplot`.
Usage

```r
make_comparison_matrix(
  in_strata_df,
  output_path = NULL,
  in_nrect = 5,
  in_attribute = "",
  in_palette = NULL
)
```

Arguments

- `in_strata_df`: Numerical data frame of all strata to be compared.
- `output_path`: Path to directory where the results, especially the figure produced by `corrplot` is going to be stored.
- `in_nrect`: Number of clusters in the clustering procedure provided by `corrplot`.
- `in_attribute`: Additional string for the file name where the figure produced by `corrplot` is going to be stored.
- `in_palette`: Colour palette for the matrix.

Value

The comparison matrix of cosine similarities.

See Also

- `compare_SMCs`

Examples

```r
data(sigs)
make_comparison_matrix(
  AlexCosmicValid_sig_df,in_nrect=9,
  in_palette=colorRampPalette(c("blue","green","red")(n=100))
)
```

make_strata_df

**Group strata from different stratification axes**

Description

For a comparison of the strata from different orthogonal stratification axes, i.e. orthogonal SMCs, the strata have to be grouped and reformatted. This function does this task for the comparison by cosine similarity of signature exposures. Output of this function is the basis for applying `plot_strata` and `make_comparison_matrix`. It is called by the wrapper functions `compare_SMCs`, `run_plot_strata_general` or `run_comparison_general`. 
Usage

make_strata_df(
    in_stratification_lists_list,
    in_remove_signature_ind = NULL,
    in_additional_stratum = NULL
)

Arguments

in_stratification_lists_list
    List of lists with entries from different (orthogonal) stratification axes or SMCs

in_remove_signature_ind
    Omit one of the signatures in in_signatures_ind_df for the comparison if non-NULL. The parameter specifies the index of the signature to be removed.

in_additional_stratum
    Include an additionally supplied stratum in comparison in non-NULL.

Value

A list with entries strata_df, number_of_SMCs, number_of_strata.

- strata_df: Pasted numerical data frame of all strata (these are going to be compared e.g. by make_comparison_matrix).
- number_of_SMCs: Number of orthogonal stratifications in in_stratification_lists_list and additional ones.
- number_of_strata: Cumulative number of strata (sum over the numbers of strata of the different stratifications in in_stratification_lists_list) and additional ones.

See Also

plot_strata
make_comparison_matrix
compare_SMCs
run_plot_strata_general
run_comparison_general

Examples

NULL
make_subgroups_df  Make a custom data structure for subgroups

Description

Creates a data frame carrying the subgroup information and the order in which the PIDs have to be displayed. Calls *aggregate* on *in_vcf_like_df*.

Usage

```r
make_subgroups_df(
  in_vcf_like_df,
  in_exposures_df = NULL,
  in_palette = NULL,
  in_subgroup.field = "SUBGROUP",
  in_PID.field = "PID",
  in_verbose = FALSE
)
```

Arguments

- `in_vcf_like_df`: vcf-like data frame with point mutation calls
- `in_exposures_df`: Data frame with the signature exposures
- `in_palette`: Palette for colour attribution to the subgroups if non-NULL
- `in_subgroup.field`: String indicating which column of `in_vcf_like_df` carries the subgroup information
- `in_PID.field`: String indicating which column of `in_vcf_like_df` and `in_exposures_df` carries the PID information
- `in_verbose`: Whether verbose or not.

Value

`subgroups_df`: A data frame carrying the subgroup and rank information.

See Also

- `aggregate`

Examples

```r
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
choice_ind <- names(lymphoma_Nature2013_COSMIC_cutoff_exposures_df) %in% unique(lymphoma_test_df$PID)
lymphoma_test_exposures_df <-
```
melt_exposures

Generically melts exposure data frames

Description
Melt an exposure data frame with signatures as ID variables.

Usage
melt_exposures(in_df)

Arguments
in_df Numeric data frame with exposures.

Value
A data frame with the molten exposures.

Examples
NULL

merge_exposures
Merge exposure data frames

Description
Merges with the special feature of preserving the signatures and signature order.

Usage
merge_exposures(in_exposures_list, in_signatures_df)

Arguments
in_exposures_list List of data frames (carrying information on exposures).
in_signatures_df Data frame in which the columns represent the signatures.
MutCat_indel_df

Value

A data frame with the merged exposures.

Examples

NULL

Description

MutCat_indel_df: A data frame in the format of a mutation catalog. The mutational catalog contains Indel variants from the GenomeOfNL_raw data. Variants were random sampled for 15 artificial patient for the purpose to have a Indel mutational catalog and have to show the functionality of the package. The results of the mutational catalog should not be interpreted for they biological relevance. Mutational catalog was created with create_indel_mutation_catalogue_from_df function.

Usage

data(GenomeOfNL_MutCat)

Value

A data frame in the layout of a Indel mutational catalog

References

Mutational catalog created form release version 5 of the Genome of NL https://www.nlgenome.nl/menu/main/app-go-nl/?page_id=9

Examples

data(GenomeOfNL_MutCat)
head(MutCat_indel_df)
dim(MutCat_indel_df)
normalizeMotifs_otherRownames

Normalize Somatic Motifs with different rownames

Description
This is a wrapper function to normalizeMotifs. The rownames are first transformed to fit the convention of the SomaticSignatures package and then passed on to the above mentioned function.

Usage
normalizeMotifs_otherRownames(in_matrix, in_norms, adjust_counts = TRUE)

Arguments
in_matrix, in_norms
Arguments to normalizeMotifs
adjust_counts Whether to rescale the counts after adaption or not. Default is true.

Value
The matrix returned by normalizeMotifs, but with rownames transformed back to the convention of the input

Examples
NULL

normalize_df_per_dim

Useful functions on data frames

Description
normalize_df_per_dim: Normalization is carried out by dividing by rowSums or colSums; for rows with rowSums=0 or columns with colSums=0, the normalization is left out.
average_over_present: If averaging over columns, zero rows (i.e. those with rowSums=0) are left out, if averaging over rows, zero columns (i.e. those with colSums=0) are left out.

sd_over_present: If computing the standard deviation over columns, zero rows (i.e. those with rowSums=0) are left out, if computing the standard deviation over rows, zero columns (i.e. those with colSums=0) are left out.

stderrmean_over_present: If computing the standard error of the mean over columns, zero rows (i.e. those with rowSums=0) are left out, if computing the standard error of the mean over rows, zero columns (i.e. those with colSums=0) are left out. Uses the function stderrmean
normalize_df_per_dim

Usage

normalize_df_per_dim(in_df, in_dimension)

average_over_present(in_df, in_dimension)

sd_over_present(in_df, in_dimension)

stderrmean_over_present(in_df, in_dimension)

Arguments

in_df Data frame to be normalized
in_dimension Dimension along which the operation will be carried out

Value

The normalized numerical data frame (normalize_df_per_dim)
A vector of the means (average_over_present)
A vector of the standard deviations (sd_over_present)
A vector of the standard errors of the mean (stderrmean_over_present)

See Also

stderrmean

Examples

test_df <- data.frame(matrix(c(1,2,3,0,5,2,3,4,0,6,0,0,0,0,4,5,6,0,7),
col=4))

## 1. Normalize over rows:
normalize_df_per_dim(test_df,1)
## 2. Normalize over columns:
normalize_df_per_dim(test_df,2)

test_df <- data.frame(matrix(c(1,2,3,0,5,2,3,4,0,6,0,0,0,0,4,5,6,0,7),
col=4))

## 1. Average over non-zero rows:
average_over_present(test_df,1)
## 2. Average over non-zero columns:
average_over_present(test_df,2)

test_df <- data.frame(matrix(c(1,2,3,0,5,2,3,4,0,6,0,0,0,0,4,5,6,0,7),
col=4))

## 1. Compute standard deviation over non-zero rows:
sd_over_present(test_df,1)
## 2. Compute standard deviation over non-zero columns:
sd_over_present(test_df,2)

test_df <- data.frame(matrix(c(1,2,3,0,5,2,3,4,0,6,0,0,0,0,4,5,6,0,7),
col=4))
## 1. Compute standard deviation over non-zero rows:
stderrmean_over_present(test_df, 1)
## 2. Compute standard deviation over non-zero columns:
stderrmean_over_present(test_df, 2)

### plotExchangeSpectra

Plot the spectra of nucleotide exchanges

#### Description
Plots the spectra of nucleotide exchanges in their triplet contexts. If several columns are present in
the input data frame, the spectra are plotted for every column separately.

#### Usage

```r
plotExchangeSpectra(
  in_catalogue_df,
  in_colour_vector = NULL,
  in_show_triplets = FALSE,
  in_show_axis_title = FALSE,
  in_scales = "free_x",
  in_refLine = NULL,
  in_refAlpha = 0.5,
  in_background = NULL
)
```

#### Arguments

- **in_catalogue_df**: Numerical data frame encoding the exchange spectra to be displayed, either a mutational catalogue V or a signatures matrix W.
- **in_colour_vector**: Specifies the colours of the 6 nucleotide exchanges if non-null.
- **in_show_triplets**: Whether or not to show the triplets on the x-axis
- **in_show_axis_title**: Whether or not to show the name of the y-axis
- **in_scales**: Argument passed on to `facet_grid`
- **in_refLine**: If non-null, value on the y-axis at which a horizontal line is to be drawn
- **in_refAlpha**: Transparency of the horizontal line if it is to be drawn
- **in_background**: Option to provide a background theme, e.g. `theme_grey`

#### Value

The generated barplot - a ggplot2 plot
See Also

- geom_bar
- facet_grid

Examples

NULL

---

plotExchangeSpectra_indel

*Plot the spectra of nucleotide exchanges of INDELs*

Description

Plots the spectra of nucleotides in their triplet contexts. If several columns are present in the input data frame, the spectra are plotted for every column separately. The function is only suitable for a INDEL spectra and for SNV representation the function `plotExchangeSpectra` should be used.

Usage

```r
plotExchangeSpectra_indel(
  in_catalogue_df,
  in_colour_vector = NULL,
  in_show_indel = FALSE,
  in_show_axis_title = FALSE,
  in_scales = "free_x",
  in_refLine = NULL,
  in_refAlpha = 0.5,
  in_background = NULL
)
```

Arguments

- `in_catalogue_df`:
  Numerical data frame encoding the exchange spectra to be displayed, either a mutational catalogue \( V \) or a signatures matrix \( W \)

- `in_colour_vector`:
  Specifies the colours of the INDELs if non-null

- `in_show_indel`:
  Whether or not to show the INDEL names on the x-axis

- `in_show_axis_title`:
  Whether or not to show the name of the y-axis

- `in_scales`:
  Argument passed on to `facet_grid`

- `in_refLine`:
  If non-null, value on the y-axis at which a horizontal line is to be drawn

- `in_refAlpha`:
  Transparency of the horizontal line if it is to be drawn

- `in_background`:
  Option to provide a background theme, e.g. `theme_grey`
plotExposuresConfidence

Value

The generated barplot - a ggplot2 plot

Examples

data(sigs_pcawg)
plotExchangeSpectra_indel(PCAWG_SP_ID_sigs_df[,c(6,8)])

plotExposuresConfidence

Plot exposures including confidence intervals

Description

Plot the exposures to extracted signatures including confidence intervals computed e.g. by variateExp.

Usage

plotExposuresConfidence(in_complete_df, in_subgroups_df, in_sigInd_df)

Arguments

  in_complete_df  Melted numeric input data frame e.g. as computed by variateExp
  in_subgroups_df Data frame containing meta information on subgroup attribution of the samples in the cohort of interest.
  in_sigInd_df    Data frame with meta information on the signatures used in the analysis.

Value

The function doesn’t return any value but plots instead.

Examples

  NULL
plotExposuresConfidence_indel

*Plot exposures including confidence intervals for exposures of SNVs and INDELs*

**Description**

Plot the exposures to extracted signatures including the confidence intervals computed e.g. by `variateExp`.

**Usage**

```r
plotExposuresConfidence_indel(in_complete_df, in_subgroups_df, in_sigInd_df)
```

**Arguments**

- `in_complete_df`: Melted numeric input data frame e.g. as computed by `variateExp`.
- `in_subgroups_df`: Data frame containing meta information on subgroup attribution of the samples in the cohort of interest.
- `in_sigInd_df`: Data frame with meta information on the signatures used in the analysis.

**Value**

The function returns a `gtable` object which can be plotted with `plot` or `grid.draw`.

**Examples**

```r
NULL
```

---

**plot_exposures**

*Plot the exposures of a cohort*

**Description**

`plot_exposures`: The exposures \( H \), determined by NMF or by `LCD`, are displayed as a stacked barplot by calling

- `geom_bar` and optionally
- `geom_text`.

The x-axis displays the PIDs (patient identifier or sample), the y-axis the counts attributed to the different signatures with their respective colours per PID. Is called by `plot_relative_exposures`.

`plot_relative_exposures`: Plot the relative or normalized exposures of a cohort. This function first normalizes its input and then sends the normalized data to `plot_exposures`. 
Usage

plot_exposures(
    in_exposures_df,
    in_signatures_ind_df,
    in_subgroups_df = NULL,
    in_sum_ind = NULL,
    in_subgroups.field = "subgroup",
    in_title = "",
    in_labels = TRUE,
    in_show_subgroups = TRUE,
    legend_height = 10
)

plot_relative_exposures(
    in_exposures_df,
    in_signatures_ind_df,
    in_subgroups_df,
    in_sum_ind = NULL,
    in_subgroups.field = "subgroup",
    in_title = "",
    in_labels = TRUE,
    in_show_subgroups = TRUE
)

Arguments

in_exposures_df  Numerical data frame encoding the exposures H, i.e. which signature contributes how much to which PID (patient identifier or sample).
in_signatures_ind_df  A data frame containing meta information about the signatures
in_subgroups_df  A data frame indicating which PID (patient or sample identifier) belongs to which subgroup
in_sum_ind  Index vector influencing the order in which the PIDs are going to be displayed
in_subgroups.field  String indicating the column name in in_subgroups_df to take the subgroup information from.
in_title  Title for the plot to be created.
in_labels  Flag, if TRUE the PIDs are displayed on the x-axis
in_show_subgroups  Flag, if TRUE then PIDs are grouped by subgroups
legend_height  How many signatures should be displayed in one column together at most.

Value

The generated barplot - a ggplot2 plot
See Also

LCD
geom_bar
geom_text

Examples

data(lymphoma_cohort_LCD_results)
plot_exposures(lymphoma_Nature2013_COSMIC_cutoff_exposures_df,
chosen_signatures_indices_df,
COSMIC_subgroups_df)

data(lymphoma_cohort_LCD_results)
plot_relative_exposures(lymphoma_Nature2013_COSMIC_cutoff_exposures_df,
chosen_signatures_indices_df,
COSMIC_subgroups_df)

Description

Plot a big composite figure with 3 columns: in the left column the per-PID absolute exposures will be shown, in the middle column the per_PID relative or normalized exposures will be shown, in the right column the cohort-wide exposures are shown (averaged over PIDs).

Usage

plot_SMC(
  number_of_strata,  # number of strata
  output_path,      # output path
  decomposition_method,  # decomposition method
  number_of_sigs,  # number of signatures
  name_list,       # name list
  exposures_strata_list,  # exposures strata list
  this_signatures_ind_df, # this signatures indices dataframe
  this_subgroups_df, # this subgroups dataframe
  in_strata_order_ind,  # in strata order indices
  exposures_both_rel_df_list,  # exposures both rel df list
  cohort_method_flag,  # cohort method flag
  fig_width = 1200,  # figure width
  fig_height = 900,  # figure height
  fig_type = "png",  # figure type
  in_label_orientation = "turn",  # in label orientation
  this_sum_ind = NULL  # this sum indices
)
plot_SMC

Arguments

number_of_strata
Number of strata as deduced from \texttt{SMC}.

output_path
Path to file where the results are going to be stored. If NULL, the results will be plotted to the running environment.

decomposition_method
String for the filename of the generated barplot.

number_of_sigs
Number of signatures.

name_list
Names of the constructed strata.

exposures_strata_list
The list of strata specific exposures $H_i$, all are numerical data frames with $l$ rows and $m$ columns, $l$ being the number of signatures and $m$ being the number of samples.

this_signatures_ind_df
A data frame containing meta information about the signatures.

this_subgroups_df
A data frame indicating which PID (patient or sample identifier) belongs to which subgroup.

in_strata_order_ind
Index vector defining reordering of the strata.

exposures_both_rel_df_list
A list of strata specific cohortwide (i.e. averaged over cohort) normalized exposures.

cohort_method_flag
Either or several of c("all_PIDs", "cohort", "norm_PIDs"), representing alternative ways to average over the cohort.

fig_width
Width of the figure to be plotted.

fig_height
Height of the figure to be plotted.

fig_type
\texttt{png} or \texttt{pdf}.

in_label_orientation
Whether or not to turn the labels on the x-axis.

this_sum_ind
Optional set of indices for reordering the PIDs.

Value

The function doesn’t return any value.

Examples

\texttt{NULL}
plot_strata  

Plot all strata from different stratification axes together

Description
Plot the cohort wide signature exposures of all strata from different stratification axes together. Naturally called by compare_SMCs.

Usage

```r
plot_strata(
  in_strata_list,
  in_signatures_ind_df,
  output_path = NULL,
  in_attribute = ""
)
```

Arguments

- `in_strata_list`: Data structure created by `make_strata_df` or `make_catalogue_strata_df` in which the strata from different orthogonal stratification axes are reorganized in a consistent structure.
- `in_signatures_ind_df`: A data frame containing meta information about the signatures.
- `output_path`: Path to directory where the results, especially the figure produced, are going to be stored.
- `in_attribute`: Additional string for the file name where the figure output is going to be stored.

Value
The function doesn’t return any value.

See Also

- `compare_SMCs`

Examples

```r
NULL
```
**Description**

Note: this function uses `read.csv` to read vcf-like files into data frames for single samples. As it uses `read.csv`, the default value for `comment.char` is "" and not "#" as it would have been for `read.table`.

**Usage**

```r
read_entry(
  current_ind, # Index of the file to read from the list provided below.
  in_list,      # List of paths to vcf-like file to be read. The list may be named.
  header = TRUE, # Boolean whether a header information should be read (as in `read.table`)
  in_header = NULL, # Vector of column names to be substituted if non-NULL.
  variant_type = "SNV", # Default is "SNV" and provides additional plausibility and checks, omitted if other string
  delete.char = NULL, # Character to be deleted, e.g. in order to discriminate between comment lines
  ...               # Parameters passed on to `read.table`
)

read_list(in_list, in_parallel = FALSE, header = TRUE, in_header = NULL, ...)
```

**Arguments**

- `current_ind`: Index of the file to read from the list provided below.
- `in_list`: List of paths to vcf-like file to be read. The list may be named.
- `header`: Boolean whether a header information should be read (as in `read.table`).
- `in_header`: Vector of column names to be substituted if non-NULL.
- `variant_type`: Default is "SNV" and provides additional plausibility and checks, omitted if other string.
- `delete.char`: Character to be deleted, e.g. in order to discriminate between comment lines and header lines, if non-NULL.
- `in_parallel`: If multicore functionality is provided on a compute cluster, this option may be set to TRUE in order to enhance speed.

**Value**

A vcf-like data frame

A list with entries:

- `vcf_like_df_list`: List of the read data frames
- `readVcf_time`: Object of class `proc.time`, which stores the time needed for reading in the data
relateSigs

Description

Make unique assignments between a set of given signatures and a set of new signatures.

Usage

relateSigs(querySigs, subjectSigs)

Arguments

querySigs The signatures to compare to (given signatures).
subjectSigs The signatures to be compared (new signatures).

Value

A list of comparison vectors

See Also

compare_sets
disambiguateVector

Examples

NULL
**repeat_df**

Create a data frame with default values

**Usage**

```
repeat_df(in_value, in_rows, in_cols)
```

**Arguments**

- `in_value` Default entry to be repeated in the data frame
- `in_rows, in_cols` Dimensions of the data frame to be created

**Value**

The created data frame

**Examples**

```
## 1. Initialize with numeric value:
repeat_df(1,2,3)
## 2. Initialize with NA value:
repeat_df(NA,3,2)
## 3. Initialize with character:
repeat_df("a",4,3)
```

---

**round_precision**

Round to a defined precision

**Description**

This function is an extension with regard to the function `round` from base R as it allows not only digits as precision, but can also round to a user-specified precision. The interval in which the rounding operation is to be carried out also can be specified by the user (default is the unit interval). Alternatively, breaks can be provided.

**Usage**

```
round_precision(x, breaks = NULL, in_precision = 0.05, in_interval = c(0, 1))
```
Arguments

- **x**  
  Vector to be rounded

- **breaks**  
  The breaks used for rounding. Default NULL

- **in_precision**  
  Precision default 0.05

- **in_interval**  
  Interval needs to be larger than the precision value

Value

A list with two entries:

- **values**: the rounded vector
- **breaks**: the breaks used for rounding

Examples

NULL

---

**run_annotate_vcf_pl**  
*Wrapper function to annotate additional information*

**Description**

Wrapper function to the perl script `annotate_vcf.pl` which annotates data of a track stored in file_B (may be different formats) to called variants stored in a vcf-like file_A.

**Usage**

```r
run_annotate_vcf_pl(
  in_data_file,  
in_anno_track_file,  
in_new_column_name,  
out_file,  
in_data_file_type = "custom",  
in_anno_track_file_type = "bed",  
in_data_CHROM.field = "CHROM",  
in_data_POS.field = "POS",  
in_data_END.field = "POS"
)
```
run_comparison_catalogues

Arguments

in_data_file Path to the input vcf-like file to be annotated
in_anno_track_file Path to the input file containing the annotation track
in_new_column_name String indicating the name of the column to be created for annotation.
out_file Path where the created files can be stored.
in_data_file_type custom for vcf-like
in_anno_track_file_type Type of the file in_anno_track_file containing the annotation track.
in_data_CHROM.field String indicating which column of in_data_file contains the chromosome information.
in_data_POS.field String indicating which column of in_data_file contains the position information.
in_data_END.field String indicating which column of in_data_file contains the end information if regions are considered.

Value

Return zero if no problems occur.

Examples

NULL

run_comparison_catalogues

Compare all strata from different stratifications

Description

Compare all strata from different orthogonal stratification axes, i.e. orthogonal SMCs by cosine similarity of mutational catalogues. Function similar to run_comparison_general. First calls

- make_catalogue_strata_df, then
- make_comparison_matrix
run_comparison_general

Usage

```r
run_comparison_catalogues(
  in_stratification_lists_list,
  output_path = NULL,
  in_nrect = 5,
  in_attribute = ""
)
```

Arguments

- `in_stratification_lists_list`: List of lists with entries from different (orthogonal) stratification axes or SMCs.
- `output_path`: Path to directory where the results, especially the figure produced by `corrplot`, is going to be stored.
- `in_nrect`: Number of clusters in the clustering procedure provided by `corrplot`.
- `in_attribute`: Additional string for the file name where the figure produced by

Value

The comparison matrix of cosine similarities.

See Also

- `make_comparison_matrix`
- `run_comparison_general`

Examples

```r
NULL
```

Description

Compare all strata from different orthogonal stratification axes, i.e. orthogonal SMCs by cosine similarity of signature exposures. Function similar to `compare_SMCs`, but without calling `plot_strata`. First calls

- `make_strata_df`, then
- `make_comparison_matrix`
run_comparison_general

Usage

run_comparison_general(
  in_stratification_lists_list,
  output_path = NULL,
  in_nrect = 5,
  in_attribute = "",
  in_remove_signature_ind = NULL,
  in_additional_stratum = NULL
)

Arguments

in_stratification_lists_list
  List of lists with entries from different (orthogonal) stratification axes or SMCs
output_path
  Path to directory where the results, especially the figure produced by corrplot is going to be stored.
in_nrect
  Number of clusters in the clustering procedure provided by corrplot
in_attribute
  Additional string for the file name where the figure produced by corrplot is going to be stored.
in_remove_signature_ind
  Omit one of the signatures in in_signatures_ind_df for the comparison if non-NULL. The parameter specifies the index of the signature to be removed.
in_additional_stratum
  Include an additionally supplied stratum in comparison in non-NULL.

Value

The comparison matrix of cosine similarities.

See Also

make_comparison_matrix
compare_SMCs
run_comparison_catalogues

Examples

NULL
run_kmer_frequency_correction

Provide comprehensive correction factors for kmer content

Description

This function is analogous to normalizeMotifs. If an analysis of mutational signatures is performed on e.g. Whole Exome Sequencing (WES) data, the signatures and exposures have to be adapted to the potentially different kmer (trinucleotide) content of the target capture. The present function takes as arguments paths to the used reference genome and target capture file. It then extracts the sequence of the target capture by calling bedtools getfasta on the system command prompt. run_kmer_frequency_normalization then calls a custom made perl script kmer_frequencies.pl also included in this package to count the occurrences of the triplets in both the whole reference genome and the created target capture sequence. These counts are used for normalization as in normalizeMotifs. Note that kmerFrequency provides a solution to approximate kmer frequencies by random sampling. As opposed to that approach, the function described here deterministically counts all occurrences of the kmers in the respective genome.

Usage

```r
run_kmer_frequency_correction(
  in_ref_genome_fasta,
  in_target_capture_bed,
  in_word_length,
  project_folder,
  target_capture_fasta = "targetCapture.fa",
  in_verbose = 1
)
```

Arguments

- `in_ref_genome_fasta`: Path to the reference genome fasta file used.
- `in_target_capture_bed`: Path to a bed file containing the information on the used target capture. May also be a compressed bed.
- `in_word_length`: Integer number defining the length of the features or motifs, e.g. 3 for tripletts or 5 for pentamers.
- `project_folder`: Path where the created files, especially the fasta file with the sequence of the target capture and the count matrices, can be stored.
- `target_capture_fasta`: Name of the fasta file of the target capture to be created if not yet existent.
- `in_verbose`: Verbose if in_verbose=1.
Value

A list with 2 entries:

- rel_cor: The correction factors after normalization as in `run_kmer_frequency_normalization`
- abs_cor: The correction factors without normalization.

See Also

`normalizeMotifs`

Examples

NULL

---

`run_kmer_frequency_normalization`

*Provide normalized correction factors for kmer content*

Description

This function is analogous to `normalizeMotifs`. If an analysis of mutational signatures is performed on e.g. Whole Exome Sequencing (WES) data, the signatures and exposures have to be adapted to the potentially different kmer (trinucleotide) content of the target capture. The present function takes as arguments paths to the used reference genome and target capture file. It the extracts the sequence of the target capture by calling `bedtools getfasta` on the system command prompt. `run_kmer_frequency_normalization` then calls a custom made perl script `kmer_frequencies.pl` also included in this package to count the occurrences of the triplets in both the whole reference genome and the created target capture sequence. These counts are used for normalization as in `normalizeMotifs`. Note that `kmerFrequency` provides a solution to approximate kmer frequencies by random sampling. As opposed to that approach, the function described here deterministically counts all occurrences of the kmers in the respective genome.

Usage

```r
run_kmer_frequency_normalization(
  in_ref_genome_fasta,
  in_target_capture_bed,
  in_word_length,
  project_folder,
  in_verbose = 1
)
```
run_plot_strata_general

Arguments

in_ref_genome_fasta
Path to the reference genome fasta file used.
in_target_capture_bed
Path to a bed file containing the information on the used target capture. May also be a compressed bed.
in_word_length
Integer number defining the length of the features or motifs, e.g. 3 for tripletts or 5 for pentamers
project_folder
Path where the created files, especially the fasta file with the sequence of the target capture and the count matrices, can be stored.
inVerbose
Verbose if inVerbose=1

Value
A numeric vector with correction factors

See Also

normalizeMotifs

Examples

NULL

run_plot_strata_general

Wrapper function for plot_strata

Description

First calls

• make_strata_df, then
• plot_strata

Usage

run_plot_strata_general(
in_stratification_lists_list,
in_signatures_ind_df,
output_path = NULL,
in_attribute = "",
in_remove_signature_ind = NULL,
in_additional_stratum = NULL
)
run_SMC

Arguments

in_stratification_lists_list
List of lists with entries from different (orthogonal) stratification axes or SMCs

in_signatures_ind_df
A data frame containing meta information about the signatures

output_path
Path to directory where the results, especially the figure produced by plot_strata is going to be stored.

in_attribute
Additional string for the file name where the figure produced by plot_strata is going to be stored.

in_remove_signature_ind
Omit one of the signatures in in_signatures_ind_df for the comparison if non-NULL. The parameter specifies the index of the signature to be removed.

in_additional_stratum
Include an additionally supplied stratum in comparison in non-NULL.

Value

The function doesn’t return any value.

See Also

plot_strata

Examples

NULL

run_SMC

Wrapper function for the Stratification of a Mutational Catalogue

Description

run_SMC takes as input a big dataframe constructed from a vcf-like file of a whole cohort. This wrapper function calls custom functions to construct a mutational catalogue and stratify it according to categories indicated by a special column in the input dataframe:

• create_mutation_catalogue_from_df
• adjust_number_of_columns_in_list_of_catalogues

This stratification yields a collection of stratified mutational catalogues, these are reformatted and sent to the custom function SMC and thus indirectly to LCD_SMC to perform a signature analysis of the stratified mutational catalogues. The result is then handed over to plot_SMC for visualization.
Usage

run_SMC(
  my_table,
  this_signatures_df,
  this_signatures_ind_df,
  this_subgroups_df,
  column_name,
  refGenome,
  cohort_method_flag = "all_PIDs",
  in_strata_order_ind = seq_len(length(unique(my_table[, column_name]))),
  wordLength = 3,
  verbose_flag = 1,
  target_dir = NULL,
  strata_dir = NULL,
  output_path = NULL,
  in_all_exposures_df = NULL,
  in_rownames = c(),
  in_norms = NULL,
  in_label_orientation = "turn",
  this_sum_ind = NULL
)

Arguments

my_table A big dataframe constructed from a vcf-like file of a whole cohort. The first
  columns are those of a standard vcf file, followed by an arbitrary number of
  custom or user defined columns. One of these must carry a PID (patient or
  sample identifyier) and one must be the category used for stratification.

this_signatures_df A numeric data frame \( \mathbf{W} \) in with \( n \) rows and \( l \) columns, \( n \) being the number of
  features and \( l \) being the number of signatures

this_signatures_ind_df A data frame containing meta information about the signatures

this_subgroups_df A data frame indicating which PID (patient or sample identifyier) belongs to
  which subgroup

column_name Name of the column in my_table which is going to be used for stratification

refGenome FaFile of the reference genome to extract the motif context of the variants in
  my_table

cohort_method_flag Either or several of c("all_PIDs", "cohort", "norm_PIDs"). representing alternative ways to average over the cohort.

in_strata_order_ind Index vector defining reordering of the strata

wordLength Integer number defining the length of the features or motifs, e.g. 3 for tripletts
  or 5 for pentamers
verbose_flag  Verbose if verbose_flag=1

target_dir   Path to directory where the results of the stratification procedure are going to be stored if non-NULL.

strata_dir   Path to directory where the mutational catalogues of the different strata are going to be stored if non-NULL.

output_path Path to directory where the results, especially the figures produced by plot_SMC are going to be stored.

in_all_exposures_df Optional argument, if specified, H, i.e. the overall exposures without stratification, is set to equal in_all_exposures_df. This is equivalent to forcing the LCD_SMC procedure to use e.g. the exposures of a previously performed NMF decomposition.

in_rownames Optional parameter to specify rownames of the mutational catalogue V i.e. the names of the features.

in_norms If specified, vector of the correction factors for every motif due to differing trinucleotide content. If null, no correction is applied.

in_label_orientation Whether or not to turn the labels on the x-axis.

this_sum_ind Optional set of indices for reordering the PIDs

Value

A list with entries exposures_list, catalogues_list, cohort and name_list.

- exposures_list: The list of s strata specific exposures Hi, all are numerical data frames with l rows and m columns, l being the number of signatures and m being the number of samples
- catalogues_list: A list of s strata specific cohortwide (i.e. averaged over cohort) normalized exposures
- cohort: subgroups_df adjusted for plotting
- name_list: Names of the constructed strata.

See Also

create_mutation_catalogue_from_df
normalizeMotifs_otherRownames
plot_SMC

Examples

library(BSgenome.Hsapiens.UCSC.hg19)
data(sigs)
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
strata_list <-
cut_breaks_as_intervals(lymphoma_test_df$random_norm,
in_outlier_cutoffs=c(-4,4),
```r
in_cutoff_ranges_list = list(c(-2.5,-1.5),
                           c(0.5,1.5)),
in_labels=c("small","intermediate","big"))
lymphoma_test_df$random_cat <- strata_list$category_vector
choice_ind <- (names(lymphoma_Nature2013_COSMIC_cutoff_exposures_df)
               %in% unique(lymphoma_test_df$PID))
lymphoma_Nature2013_COSMIC_cutoff_exposures_df <-
lymphoma_Nature2013_COSMIC_cutoff_exposures_df[,choice_ind]
temp_subgroups_df <- make_subgroups_df(lymphoma_test_df,
                         lymphoma_test_exposures_df)
mut_density_list <- run_SMC(lymphoma_test_df,
                         AlexCosmicValid_sig_df,
                         AlexCosmicValid_sigInd_df,
                         temp_subgroups_df,
                         column_name="random_cat",
                         refGenome=BSgenome.Hsapiens.UCSC.hg19,
                         cohort_method_flag="norm_PIDs",
                         in_rownames = rownames(AlexCosmicValid_sig_df))
```

### shapiro_if_possible

Wrapper for Shapiro test but allow for all identical values

**Description**

Wrapper for Shapiro test but allow for all identical values

**Usage**

```r
shapiro_if_possible(in_vector)
```

**Arguments**

- `in_vector` Numerical vector the Shapiro-Wilk test is computed on

**Value**

p-value of the Shapiro-Wilk test, zero if all entries in the input vector `in_vector` are identical.

**See Also**

- `shapiro.test`

**Examples**

```r
shapiro_if_possible(runif(100,min=2,max=4))
shapiro_if_possible(rnorm(100,mean=5,sd=3))
shapiro_if_possible(rep(4.3,100))
shapiro_if_possible(c("Hello","World"))
```
Description

The numerical data of the mutational signatures published initially by Alexandrov et al. (Nature 2013) and Alexandrov et al., (Bioaxiv 2018) is stored in data frames with endings _sig_df, the associated meta-information is stored in data frames with endings _sigInd_df. There are several instances of _sig_df and _sigInd_df, corresponding to results and data obtained at different times and with different raw data. There always is a one-to-one correspondence between a _sig_df and a _sigInd_df. The data frames of type _sig_df have as many rows as there are features, i.e. 96 if analyzing mutational signatures of SNVs in a triplet context, and as many columns as there are signatures. Data frames of type _sigInd_df have as many rows as there are signatures in the corresponding _sig_df and several columns:

- sig: signature name
- index: corresponding to the row index of the signature
- colour: colour for visualization in stacked barplots
- process: asserted biological process
- cat.coarse: categorization of the signatures according to the asserted biological processes at low level of detail
- cat.medium: categorization of the signatures according to the asserted biological processes at intermediate level of detail
- cat.high: categorization of the signatures according to the asserted biological processes at high level of detail
- cat.putative: categorization of the signatures according to the asserted biological processes based on clustering and inference

Please note, that categorization columns are only present for the data frames corresponding to the data from Alexandrov et al. (Nature 2013).

AlexInitialArtif_sig_df: Data frame of the signatures published initially by Alexandrov et al. (Nature 2013). There are 27 signatures which constitute the columns, 22 of which were validated by an orthogonal sequencing technology. These 22 are in the first 22 columns of the data frame. The column names are A pasted to the number of the signature, e.g. A5. The nonvalidated signatures have an additional letter in their naming convention: either AR1 - AR3 or AU1 - AU2. The rownames are the features, i.e. an encoding of the nucleotide exchanges in their trinucleotide context, e.g. C>A ACA. In total there are 96 different features and therefore 96 rows when dealing with a trinucleotide context.

AlexInitialArtif_sigInd_df: Meta-information for AlexInitialArtif_sig_df

AlexInitialValid_sig_df: Data frame of only the validated signatures published initially by Alexandrov et al. (Nature 2013), corresponding to the first 22 columns of AlexInitialArtif_sig_df

AlexInitialValid_sigInd_df: Meta-information for AlexInitialValid_sig_df

AlexCosmicValid_sig_df: Data frame of the updated signatures list maintained by Ludmil Alexandrov at https://cancer.sanger.ac.uk/cosmic/signatures. The column names are AC pasted
to the number of the signature, e.g. AC5. The naming convention for the rows is as described for `AlexInitialArtif_sig_df`.

AlexCosmicValid_sigInd_df: Meta-information for `AlexCosmicValid_sig_df`

AlexCosmicArtif_sig_df: Data frame of the updated signatures list maintained by Ludmil Alexandrov at [https://cancer.sanger.ac.uk/cosmic/signatures](https://cancer.sanger.ac.uk/cosmic/signatures) and complemented by the artifact signatures from the initial publication, i.e. the last 5 columns of `AlexInitialArtif_sig_df`. The column names are AC pasted to the number of the signature, e.g. AC5. The naming convention for the rows is as described for `AlexInitialArtif_sig_df`.

AlexCosmicArtif_sigInd_df: Meta-information for `AlexCosmicArtif_sig_df`

**Usage**

```r
data(sigs)
```

**Author(s)**

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

**Source**

AlexInitial: [ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/signatures.txt](ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/signatures.txt)

AlexCosmic: [https://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt](https://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt)

**References**

Alexandrov et al. (Nature 2013)
Description

PCAWG_SP_SBS_sigInd_Artif_df: Meta-information for PCAWG_SP_SBS_sigs_Artif_df

PCAWG_SP_SBS_sigs_Real_df: Data frame of only the validated signatures published by Alexandrov et al. (Biorxiv 2018), corresponding to the column 1-26, 28-42 and 44 of the PCAWG_SP_SBS_sigs_Artif_df data frame

PCAWG_SP_SBS_sigInd_Real_df: Meta-information for PCAWG_SP_SBS_sigs_Real_df

PCAWG_SP_ID_sigs_df: Data frame with Indel signatures published by Alexandrov et al. (Biorxiv 2018) which were decomposed with the method SigProfiler. There are 17 Sigantures reported but as supervised signatures are only valid for whole genome sequencing data analysis. In whole genome sequencing data the Indel signature ID15 was not discribed and thus is not part of this data set. In total 83 features are described. The categorization considers the size of the insertion and delition, the motif, and the sequence context. Hereby the number of repetition or patial repetition of the motif is determined.

PCAWG_SP_ID_sigInd_df: Meta-information for PCAWG_SP_ID_sigs_df

Usage

data(sigs_pcawg)

Author(s)

Lea Jopp-Suile <huebschmann.daniel@googlemail.com>

Source

PCAWG_SNV: https://www.synapse.org/#!Synapse:syn11738319
PCAWG_INDEL: https://cancer.sanger.ac.uk/cosmic/signatures/ID

References

Alexandrov et al. (Biorxiv 2018)

SMC

Stratification of a Mutational Catalogue

Description

SMC takes a given collection of stratified mutational catalogues Vi, sends them to perform a mutational signatures decomposition by Linear Combination Decomposition (LCD) with the functions LCD_SMC with known signatures W. It subsequently performs some useful statistics and preparation for plotting with the function plot_SMC. SMC is naturally called by run_SMC.
Usage

SMC(
  df_list,
  this_signatures_df,
  in_all_exposures_df,
  number_of_strata,
  number_of_sigs,
  name_list,
  this_subgroups_df,
  mutation_catalogue_all_df,
  cohort_method_flag,
  in_verbose = 1
)

Arguments

  df_list         A list of $s$ stratified mutational catalogues $V_i \ (\text{numeric data frames})$ with $n$ rows and $m$ columns each, $n$ being the number of features and $m$ being the number of samples. This list is naturally provided in run_SMC.
  this_signatures_df
                   A numeric data frame $W$ with $n$ rows and $1$ columns, $n$ being the number of features and $1$ being the number of signatures
  in_all_exposures_df
                   The overall exposures $H$ without stratification, a numeric data frame with $l$ rows and $m$ columns, $l$ being the number of signatures and $m$ being the number of samples
  number_of_strata
                   The length of the list df_list
  number_of_sigs
                   The number of signatures used in the current decomposition.
  name_list
                   A list of names of the different strata
  this_subgroups_df
                   A data frame indicating which PID (patient or sample identifyier) belongs to which subgroup
  mutation_catalogue_all_df
                   The overall mutational catalogue $V$ without stratification.
  cohort_method_flag
                   Either or several of c("all_PIDs", "cohort", "norm_PIDs"), representing alternative ways to average over the cohort.
  in_verbose
                   Verbose if in_verbose=1

Value

A list with entries exposures_strata_list, exposures_both_rel_df_list, this_subgroups_df, subgroup_ind and decomposition_method.

- exposures_strata_list: The list of $s$ strata specific exposures $H_i$, all are numerical data frames with $l$ rows and $m$ columns, $l$ being the number of signatures and $m$ being the number of samples
• exposures_both_rel_df_list: A list of strata specific cohortwide (i.e. averaged over cohort) normalized exposures
• this_subgroups_df: subgroups_df adjusted for plotting
• subgroup_ind: Index of the subgroups chosen and relevant for plotting.
• decomposition_method: String telling whether LCD or NMF was used, relevant only for handing over to plot_SMC.

See Also
run_SMC
plot_SMC
LCD_SMC

Examples
NULL

SMC_perPID

Run SMC at a per sample level

Description
Run an SMC analysis (stratification of the mutational catalogue) at per sample / per-PID level, corresponding to a divide and conquer strategy. For every single PID, only those signatures actually present in this PID will be provided for the SMC analysis.

Usage
SMC_perPID(
  in_dfList,
  in_LCDlist,
  in_subgroups_df,
  in_save_plot = TRUE,
  in_save_dir = NULL,
  in_save_name = "KataegisSMCs.pdf",
  in_verbose_flag = 0,
  ...
)

Arguments
in_dfList Named list of vcf-like data frames, one entry per sample/PID of a cohort.
in_LCDlist Output of an LCD list performed on the above cohort, carrying notably information on the exposures (in_LCDlist$exposures), the present signatures (in_LCDlist$sigures) and meta information about the signatures(in_LCDlist$out_sig_ind_df).
split_exposures_by_subgroups

**Description**

If a cohort consists of different subgroups, this function enables to split the data frame storing the signature exposures into a list of data frames with signature exposures, one per subgroup. This functionality is needed for `stat_test_subgroups` and `stat_plot_subgroups`.

**Usage**

```r
split_exposures_by_subgroups(
  in_exposures_df,
  in_subgroups_df,
  in_subgroups.field = "subgroup",
  in_PID.field = "PID"
)
```

**Arguments**

- `in_exposures_df`  
  Numerical data frame of the exposures (i.e. contributions of the different signatures to the number of point mutations per PID)

- `in_subgroups_df`  
  Data frame indicating which PID belongs to which subgroup

**Value**

A list of lists. The top level is a named per-PID list, each entry is of type SMClst (cf. `run_SMC`).

**Examples**

```r
NULL
```
stat_plot_subgroups

in_subgroups.field
Name indicating which column in in_subgroups_df contains the subgroup information

in_PID.field
Name indicating which column in in_subgroups_df contains the PID information

Value
List of data frames with the subgroup specific signature exposures.

See Also
stat_test_subgroups
stat_plot_subgroups

Examples

NULL

Description
Plot one averaged signature exposure pattern per subgroup. Uses split_exposures_by_subgroups.

Usage

stat_plot_subgroups(
  in_exposures_df,
  in_subgroups_df,
  in_signatures_ind_df,
  in_subgroups.field = "subgroup",
  in_PID.field = "PID",
  in_colour_vector = NULL
)

Arguments

in_exposures_df
Numerical data frame of the exposures (i.e. contributions of the different signatures to the number of point mutations per PID)

in_subgroups_df
Data frame indicating which PID belongs to which subgroup

in_signatures_ind_df
Data frame carrying additional information on the signatures
stat_test_SMC

in_subgroups.field
  Name indicating which column in in_subgroups_df contains the subgroup information

in_PID.field
  Name indicating which column in in_subgroups_df contains the PID information

in_colour_vector
  If non-null, specifies the colours attributed to the subgroups

Value

The function doesn’t return any value, it plots instead.

See Also

split_exposures_by_subgroups

Examples

NULL

stat_test_SMC

Apply statistical tests to a stratification (SMC)

Description

stat_test_SMC tests for enrichment or depletion in the different strata of a stratification of the mutational catalogue for every signature independently by applying Kruskal Wallis tests. For those signatures where the Kruskal Wallis test gives a significant p-value, pairwise posthoc tests are carried out by calling kwAllPairsNemenyiTest. Additionally all data is tested for normality by Shapiro Wilk tests, so that the user may apply ANOVA and pairwise posthoc t-test where allowed.

Usage

stat_test_SMC(in_strat_list, in_flag = "norm")

Arguments

in_strat_list  A list with entries exposures_list, catalogues_list, cohort and name_list as in the output of run_SMC:
  • exposures_list: The list of s strata specific exposures Hi, all are numerical data frames with l rows and m columns, l being the number of signatures and m being the number of samples
  • catalogues_list: A list of s strata specific cohortwide (i.e. averaged over cohort) normalized exposures
  • cohort: subgroups_df adjusted for plotting
  • name_list: Names of the contracted strata.

in_flag  If "norm", all tests are performed on normalized exposures, otherwise the absolute exposures are taken.
Value

A list with entries `kruskal_df`, `shapiro_df`, `kruskal_posthoc_list`,

- `kruskal_df`: A data frame containing results (statistic and p values) of the Kruskal Wallis tests (tests for enrichment or depletion in the different strata for every signature independently).
- `shapiro_df`: A data frame containing results (p values) of the Shapiro Wilk tests (tests for normal distribution in the different strata for every signature independently).
- `kruskal_posthoc_list`: A list of results of pairwise posthoc tests carried out for those signatures where the Kruskal Wallis test yielded a significant p-value (carried out by `kwAllPairsNemenyiTest`).

See Also

`run_SMC`  
`kwAllPairsNemenyiTest`  
`kruskal.test`  
`shapiro_if_possible`  
`shapiro.test`

Examples

```r
NULL
```
(stderrmean)

Arguments

- `in_exposures_df`  
  Numerical data frame of the exposures (i.e. contributions of the different signatures to the number of point mutations per PID)

- `in_subgroups_df`  
  Data frame indicating which PID belongs to which subgroup

- `in_subgroups.field`  
  Name indicating which column in `in_subgroups_df` contains the subgroup information

- `in_PID.field`  
  Name indicating which column in `in_subgroups_df` contains the PID information

Value

A list with entries `kruskal_df`, `kruskal_posthoc_list`,

- `kruskal_df`: A data frame containing results (statistic and p values) of the Kruskal Wallis tests (tests for enrichment or depletion in the different strata for every signature independently).

- `kruskal_posthoc_list`: A list of results of pairwise posthoc tests carried out for those signatures where the Kruskal Wallis test yielded a significant p-value (carried out by `kwAllPairsNemenyiTest`).

See Also

- `split_exposures_by_subgroups`
- `stat_test_SMC`
- `kwAllPairsNemenyiTest`
- `kruskal.test`

Examples

NULL

stderrmean  

*Compute the standard error of the mean*

Description

This function returns the standard deviation of an input numerical vector divided by the square root of the length of the input vector

Usage

`stderrmean(x)`
**sum_over_list_of_df**

**Arguments**

- **x**  
  A numerical vector

**Value**

Standard deviation of an input numerical vector divided by the square root of the length of the input vector

**Examples**

```r
A <- c(1,2,3)
sd(A)
stderrmean(A)
```

---

**sum_over_list_of_df**  
Elementwise sum over a list of (numerical) data frames

---

**Description**

Elementwise sum over a list of (numerical) data frames

**Usage**

```r
sum_over_list_of_df(in_df_list)
```

**Arguments**

- **in_df_list**  
  List of (numerical) data frames

**Value**

A numerical data frame with the same dimensions as the entries of `in_df_list` with elementwise sums

**Examples**

```r
A <- data.frame(matrix(c(1,1,1,2,2,2),ncol=2))
B <- data.frame(matrix(c(3,3,3,4,4,4),ncol=2))
df_list <- list(A=A,B=B)
sum_over_list_of_df(df_list)
```
Description

List of lists with correction factors for different target capture kits. The elements of the overall list are lists, every one carrying information for one target capture kit (and named after it). The elements of these sublists are 64 dimensional vectors with correction factors for all triplets. They were computed using counts of occurrence of the respective triplets in the target capture and in the reference genome and making ratios (either for the counts themselves as in `abs_cor` or for the relative occurrences in `rel_cor`). The information in this data structure may be used as input to `normalizeMotifs_otherRownames`.

Usage

data(targetCapture_cor_factors)

Value

A list of lists of data frames

Author(s)

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

description

# testSigs

Test for significance of alternative models cohort wide

Description

Wrapper function for `variateExpSingle` for application cohort wide.

Usage

testSigs(
    in_catalogue_df,
    in_sig_df,
    in_exposures_df,
    in_factor = 0,
    in_pdf = NULL
)
Arguments

in_catalogue_df  
Input numerical data frame of the mutational catalog of the cohort to be analyzed

in_sig_df  
Numerical data frame of the signatures used for analysis.

in_exposures_df  
Input numerical data frame of the exposures computed for the cohort to be analyzed

in_factor  
Deviation factor of the altered alternative model.

in_pdf  
Probability distribution function, parameter passed on to confIntExp if NULL assumed to be normal distribution.

Value

Returns a data frame

Examples

NULL

Description

Test significance of association between a vector of exposures and a selection of samples, e.g. those affected by mutations in a pathway as returned by find_affected_PIDs

Usage

test_exposureAffected(
  in_exposure_vector,
  in_affected_PIDs,
  in_mutation_label = NULL,
  in_exposure_label = NULL
)

Arguments

in_exposure_vector  
Named vector of a phenotype (e.g. exposures to a specific signature)

in_affected_PIDs  
Character vector of samples affected by some criterion, e.g. mutations in a pathway as returned by find_affected_PIDs

in_mutation_label  
If non-NULL, prefix to the mutation status (x-axis label) in the produced boxplot

in_exposure_label  
If non-NULL, prefix to the exposures (y-axis label) in the produced boxplot
Value

A list with entries:

- current_kruskal: Kruskal test object from testing phenotype against affection
- current_boxplot: Boxplot of phenotype against affection

Examples

NULL

test_gene_list_in_exposures

Test if mutated PIDs are enriched in signatures

Description

For all signatures found in a project, this function tests whether PIDs having mutations in a specified list of genes of interest have significantly higher exposures.

Usage

test_gene_list_in_exposures(
  in_gene_list,
  in_exposure_df,
  in_mut_table,
  in_gene.field = "GENE_short",
  in_p_cutoff = 0.05
)

Arguments

in_gene_list List with genes of interest
in_exposure_df Data frame with the signature exposures
in_mut_table Data frame or table of mutations (derived from vcf-format)
in_gene.field Name of the column in which the gene names are to be looked up
in_p_cutoff Significance threshold

Value

A list with entries pvals, exposure_df, number_of_mutated,

- pvals: p-values of the t-tests performed on mutated vs. unmutated PIDs
- exposure_df: Transposed input exposures data frame with additional annotations for mutation status
- number_of_mutated: Number of PIDs carrying a mutation
transform_rownames_R_to_MATLAB

Description

Rownames or names of the features used differ between the different contexts a signature analysis is carried out in. The function `transform_rownames_R_to_MATLAB` changes from the convention used in the YAPSA package to the one used by Alexandrov et al. in the MATLAB framework.

The function `transform_rownames_MATLAB_to_R` changes from the convention used in Alexandrov et al. in the MATLAB framework to the one used by the YAPSA package.

The function `transform_rownames_MATLAB_to_R` changes from the convention used in stored mutational catalogues by Alexandrov et al. to the one used by the YAPSA package.

The function `transform_rownames_YAPSA_to_deconstructSigs` changes from the convention used in the YAPSA package to the one used by the deconstructSigs package.

The function `transform_rownames_YAPSA_to_deconstructSigs` changes from the convention used in the deconstructSigs package to the one used by the YAPSA package.

Usage

```r
transform_rownames_R_to_MATLAB(in_rownames, wordLength = 3)
transform_rownames_MATLAB_to_R(in_rownames, wordLength = 3)
transform_rownames_nature_to_R(in_rownames, wordLength = 3)
transform_rownames_YAPSA_to_deconstructSigs(in_rownames, wordLength = 3)
transform_rownames_deconstructSigs_to_YAPSA(in_rownames, wordLength = 3)
```

Arguments

- `in_rownames`: Character vector of input rownames
- `wordLength`: Size of the considered motif context

Value

A character vector of the translated rownames.

Examples

```r
NULL
```
translate_to_hg19  
Translate chromosome names to the hg19 naming convention

Description

translate_to_hg19: In hg19 naming convention, chromosome names start with the prefix *chr* and the gonosomes are called *X* and *Y*. If data analysis is performed e.g. with `BSgenome.Hsapiens.UCSC.hg19`, this naming convention is needed. The inverse transform is done with `translate_to_1kG`.

translate_to_1kG: In 1kG, i.e. 1000 genomes naming convention, chromosome names have no prefix *chr* and the gonosomes are called 23 for *X* and 24 for *Y*. If data analysis is performed e.g. with `hs37d5.fa`, this naming convention is needed. The inverse transform is done with `translate_to_hg19`.

Usage

```r
translate_to_hg19(in_dat, in_CHROM.field = "CHROM", in_verbose = FALSE)
translate_to_1kG(in_dat, in_CHROM.field = "chr", in_verbose = FALSE)
```

Arguments

- `in_dat`  GRanges object, VRanges object or data frame which carries one column with chromosome information to be reformatted.
- `in_CHROM.field`  String indicating which column of `in_dat` carries the chromosome information
- `in_verbose`  Whether verbose or not.

Value

GRanges object, VRanges object or data frame identical to `in_dat`, but with the names in the chromosome column replaced (if dealing with data frames) or alternatively the seqlevels replaced (if dealing with GRanges or VRanges objects).

Examples

```r
test_df <- data.frame(CHROM=c(1,2,23,24),POS=c(100,120000000,30000,25000),
                      dummy=c("a","b","c","d"))
hg19_df <- translate_to_hg19(test_df, in_CHROM.field = "CHROM")
hg19_df

test_df <- data.frame(CHROM=c(1,2,23,24),POS=c(100,120000000,30000,25000),
                      dummy=c("a","b","c","d"))
hg19_df <- translate_to_hg19(test_df, in_CHROM.field = "CHROM")
onekG_df <- translate_to_1kG(hg19_df, in_CHROM.field = "CHROM")
onekG_df
```
Create a rainfall plot in a trellis structure

Description

A trellis is a plot structure which allows space optimized multi-panel multi track plots. This function uses the package `gtrellis` developed by Zuguang Gu, also available at https://www.bioconductor.org/packages/release/bioc/html/gtrellis.html. The graphics in the tracks within a gtrellis plot are mostly drawn with functions from the package `grid`. Note that for technical reasons, the column indicating the chromosome MUST have the name `chr` and be the first column in the data frame supplied to the gtrellis functions. Therefore reformatting is performed in this function before calling gtrellis functions.

Usage

trellis_rainfall_plot(
  in_rainfall_dat,
  in_point_size = unit(1, "mm"),
  in_rect_list = NULL,
  in_title = "",
  in_CHROM.field = "CHROM",
  in_POS.field = "POS",
  in_dist.field = "dist",
  in_col.field = "col"
)

Arguments

in_rainfall_dat  Data frame which has to contain at least columns for chromosome, position, intermutational distance and colour information

in_point_size  size of the points in the rainfall plot to be created has to be provided with appropriate units, e.g. `in_point_size=unit(0.5,"mm")`

in_rect_list  Optional argument, if present, will lead to highlighting of specified regions by coloured but transparent rectangles

in_title  Title in the figure to be created.

in_CHROM.field  String indicating which column of `in_rainfall_dat` carries the chromosome information

in_POS.field  String indicating which column of `in_rainfall_dat` carries the position information

in_dist.field  String indicating which column of `in_rainfall_dat` carries the intermutational distance information

in_col.field  String indicating which column of `in_rainfall_dat` carries the colour information encoding the nucleotide exchange
Value

The function doesn’t return any value.
The function doesn’t return any value.

See Also

gtrellis_layout
add_track
grid.points

Examples

data(lymphoma_test)
choice_PID <- "4121361"
PID_df <- subset(lymphoma_test_df, PID==choice_PID)
trellis_rainfall_plot(PID_df, in_point_size=unit(0.5,"mm"))

---

variateExp

Wrapper to compute confidence intervals for a cohort

Description

Wrapper function around confIntExp, which is applied to every signature/sample pair in a cohort. The extracted upper and lower bounds of the confidence intervals are added to the input data which is reordered and melted in order to prepare for visualization with ggplot2.

Usage

variateExp(
  in_catalogue_df,
  in_sig_df,
  in_exposures_df,
  in_sigLevel = 0.05,
  in_delta = 0.4,
  in_pdf = NULL
)

Arguments

  in_catalogue_df  Input numerical data frame of the mutational catalog of the cohort to be analyzed.
  in_sig_df        Numerical data frame of the signatures used for analysis.
variateExp

**in_exposures_df**
Input numerical data frame of the exposures computed for the cohort to be analyzed.

**in_sigLevel**
Significance level, parameter passed to `confIntExp`.

**in_delta**
Inflation parameter for the alternative model, parameter passed on to `confIntExp`.

**in_pdf**
Probability distribution function, parameter passed on to `confIntExp`, if NULL assumed to be normal distribution.

**Value**
A melted data frame.

**Examples**

```r
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
data(sigs)
word_length <- 3
temp_list <- create_mutation_catalogue_from_df(
  lymphoma_test_df, this_seqnames.field = "CHROM",
  this_start.field = "POS", this_end.field = "POS",
  this_PID.field = "PID", this_subgroup.field = "SUBGROUP",
  this_refGenome = BSgenome.Hsapiens.UCSC.hg19,
  this_wordLength = word_length)
lymphoma_catalogue_df <- temp_list$matrix
lymphoma_PIDs <- colnames(lymphoma_catalogue_df)
data("lymphoma_cohort_LCD_results")
lymphoma_exposures_df <-
  lymphoma_Nature2013_COSMIC_cutoff_exposures_df[, lymphoma_PIDs]
lymphoma_sigs <- rownames(lymphoma_exposures_df)
lymphoma_sig_df <- AlexCosmicValid_sig_df[, lymphoma_sigs]
lymphoma_complete_df <- variateExp(in_catalogue_df = lymphoma_catalogue_df,
  in_sig_df = lymphoma_sig_df,
  in_exposures_df = lymphoma_exposures_df,
  in_sigLevel = 0.025, in_delta = 0.4)

head(lymphoma_complete_df)
lymphoma_complete_df$sample <-
  factor(lymphoma_complete_df$sample,
    levels = colnames(lymphoma_exposures_df)[
      order(colSums(lymphoma_exposures_df), decreasing = TRUE)])
sig_colour_vector <- c("black", AlexCosmicValid_sigInd_df$colour)
names(sig_colour_vector) <-
  c("total", as.character(AlexCosmicValid_sigInd_df$sig))
ggplot(data = lymphoma_complete_df,
  aes(x = sample, y = exposure, fill = sig)) +
geom_bar(stat = "identity") +
geom_errorbar(aes(ymin = lower, ymax = upper), width = 0.2) +
facet_wrap(~sig, nrow = nrow(lymphoma_exposures_df) + 1) +
theme_grey() +
theme(panel.border = element_rect(fill = NA, colour = "black"),
```
variateExpSingle

Wrapper for the likelihood ratio test

Description

Application of the likelihood ratio test to mutational signatures, primarily for one single sample.

Usage

variateExpSingle(
  in_catalogue_vector,
  in_sig_df,
  in_exposure_vector,
  in_ind,
  in_factor = 1,
  in_pdf = NULL,
  verbose = FALSE
)

Arguments

in_catalogue_vector
  Mutational catalog of the input sample.

in_sig_df
  Data frame encoding the signatures used for the analysis.

in_exposure_vector
  Exposure vector computed for the input sample.

in_ind
  Index specifying which signature among in_sig_df is to be tested.

in_factor
  Deviation factor of the altered alternative model.

in_pdf
  Probability distribution function, parameter passed on to logLikelihood and later to computeLogLik.

verbose
  Verbose if in_verbose=1

Value

Returns a list
Examples

```r
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
data(sigs)
word_length <- 3
temp_list <- create_mutation_catalogue_from_df(  
  lymphoma_test_df, this_seqnames.field = "CHROM",  
  this_start.field = "POS", this_end.field = "POS",  
  this_PID.field = "PID", this_subgroup.field = "SUBGROUP",  
  this_refGenome = BSgenome.Hsapiens.UCSC.hg19,  
  this_wordLength = word_length)
lymphoma_catalogue_df <- temp_list$matrix
lymphoma_PIDs <- colnames(lymphoma_catalogue_df)
data("lymphoma_cohort_LCD_results")
lymphoma_exposures_df <-  
  lymphoma_Nature2013_COSMIC_cutoff_exposures_df[, lymphoma_PIDs]
lymphoma_sigs <- rownames(lymphoma_exposures_df)
lymphoma_sig_df <- AlexCosmicValid_sig_df[, lymphoma_sigs]
variateExpSingle(
  in_ind = 1,
  in_factor = 1.5,
  in_catalogue_vector = lymphoma_catalogue_df[, 1],
  in_sig_df = lymphoma_sig_df,
  in_exposure_vector = lymphoma_exposures_df[, 1])
```

Description

Yet Another Package for mutational Signature analysis

Details

This package provides functions and routines useful in the analysis of mutational signatures (cf. L. Alexandrov et al., Nature 2013). In particular, functions to perform a signature analysis with known signatures (LCD = linear combination decomposition) and a signature analysis on stratified mutational catalogue (run_SMC = stratify mutational catalogue) are provided.
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