

# Package ‘YAPSA’

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**Depends** R (>= 4.0.0), GenomicRanges, ggplot2, grid

**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., *BioRxiv* 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.

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<b>add_annotation</b>	<i>Add information to an annotation data structure</i>
-----------------------	--

---

## Description

Function to iteratively add information to an annotation data structure as needed for [HeatmapAnnotation](#) and especially for [annotation\\_exposures\\_barplot](#)

## Usage

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

## Arguments

<b>in_annotation_col</b>	List, every element of which refers to one layer of annotation
	List elements are structures corresponding to named colour vectors
<b>in_annotation_df</b>	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 <b>in_annotation_df</b> correspond to the names of the corresponding element in <b>in_annotation_col</b>
<b>in_attribution_vector</b>	A vector which is going to be cbinded to <b>in_annotation_df</b> , carrying the annotation information of the new layer to be added
<b>in_colour_vector</b>	Named vector of colours to be attributed to the new annotation
<b>in_name</b>	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

**Value**

List with input element as first entry.

**Examples**

NULL

---

`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  $H$ , 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 subfraction 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

```
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 <a href="#">annotate_intermut_dist_PID</a> to <a href="#">rainfallTransform</a> 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(1,1,1,2,2,2,3,3,3,4,4,4,5,5),
                       POS=c(1,2,4,4,6,9,1,4,8,10,20,40,100,200),
                       REF=c("C","C","C","T","T","T","A",
                             "A","A","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))
test_df <- test_df[order(test_df$PID,test_df$CHROM,test_df$POS),]
min_dist_df <-
  annotate_intermut_dist_cohort(test_df,in_CHROM.field="CHROM",
                                in_POS.field="POS", in_PID.field="PID",
                                in_mode="min")
max_dist_df <-
  annotate_intermut_dist_cohort(test_df,in_CHROM.field="CHROM",
                                in_POS.field="POS", in_PID.field="PID",
                                in_mode="max")
min_dist_df
max_dist_df
```

annotate\_intermut\_dist\_PID

### Annotation of the mutation 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

```
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 <code>rainfallTransform</code> 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_intermut_dist_cohort  
rainfallTransform
```

## Examples

```
max_dist_df <- annotate_intermut_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  $H$ , 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_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 <a href="#">draw</a>
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")`

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**

```
annotation_exposures_list_barplot(
  in_exposures_list,
  in_signatures_ind_list,
  in_subgroups_list,
  in_annotation_list,
  ylab = NULL,
  title = "",
  in_indel_sigs = FALSE,
  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\_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).

**in\_signatures\_ind\_list**

A list of data frame containing meta information about each signature type individually

**in\_subgroups\_list**

A list of data frame indicating of each signature type which PID (patient or sample identifier) belongs to which subgroup

<code>in_annotation_list</code>	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
<code>ylab</code>	String indicating the column name in <code>in_subgroups_df</code> to take the subgroup information from.
<code>title</code>	Title for the plot to be created.
<code>in_indel_sigs</code>	Tag which is default FALSE when whole genome data are analysed the tag will be TRUE
<code>in_labels</code>	Whether or not to show the names of the samples.
<code>in_barplot_borders</code>	Whether or not to show border lines in barplot
<code>in_column_anno_borders</code>	Whether or not to draw separating lines between the fields in the annotation
<code>in_annotation_legend_side</code>	Where to put the legends of the annotation df, default is right.
<code>in_padding</code>	Parameter passed on to function <code>draw</code>
<code>in_annotation</code>	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")`

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 $H$ , 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 <a href="#">dist</a> . Can be either of: <code>euclidean</code> , <code>maximum</code> , <code>manhattan</code> , <code>canberra</code> , <code>binary</code> or <code>minkowski</code>

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 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.

## 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 features, 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",  

  in_verbose = 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
in_verbose	Whether verbose or not.

**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**

```
test_df <- data.frame(
  CHROM=c(1,1,1,2,2,2,3,3,3,4,4,4,5,5),
  POS=c(1,2,3,4,5,6,1,2,3,4,5,6,7,8),
  REF=c("C","C","C","T","T","A","A","A","G","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
```

**attribute\_sequence\_context\_indel**

*Attribution of sequence context and size for an INDEL*

**Description**

The function is a wrapper and uses [getSequenceContext](#) to annotate the sequence context.

**Usage**

```
attribute_sequence_context_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	Verbose 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 variant. Per default 50 bps are annotated

### 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 in\_REF.field and in\_ALT.field.

### Examples

```
data(GenomeOfN1_raw)
GenomeOfN1_context <- attribute_sequence_context_indel(
  in_dat = head(GenomeOfN1_raw),
  in_REF.field = "REF",
  in_ALT.field = "ALT",
  in_verbose = FALSE,
  in_offsetL= 10, in_offsetR=50)
GenomeOfN1_context
```

---

### attribution\_of\_indels *Attribution of variant into one of the 83 INDEL categories*

---

### 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 follows:

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 insertion 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**

```
attribution_of_indels(in_dat_return = in_dat_return)
```

**Arguments**

`in_dat_return` Data frame constructed from a vcf-like file of a whole cohort or a single-sample. 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**

```
data(GenomeOfN1_raw)
GenomeOfN1_context <- attribute_sequence_context_indel(in_dat =
head(GenomeOfN1_raw))
GenomeOfN1_classified <- attribution_of_indels(GenomeOfN1_context)
GenomeOfN1_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**

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

**Arguments**

<code>in_string</code>	Name or description of the pathway
<code>in_organism</code>	Name of the taxon to be searched in

**Value**

A character vector of gene names

**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

## Value

classVector, a factor vector of indel sizes

## Examples

NULL

---

compare_exposures	<i>Compares alternative exposures</i>
-------------------	---------------------------------------

---

## Description

Compares exposures computed by two alternative approaches for the same cohort

## Usage

```
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\_exposure\_sets *Compare two sets of exposures by cosine distance*

---

## Description

Compare two sets of exposures, stored in numerical data frames H1 and H2, by computing the row-wise cosine distance

## Usage

```
compare_exposure_sets(in_df_small, in_df_big, in_distance = cosineDist)
```

## Arguments

in\_df\_small, in\_df\_big

Numerical data frames H1 and H2, ideally the bigger one first, both with 1 rows and m1 and m2 columns, 1 being the number of signatures and m1 and m2 being the respective numbers of samples or patient identifier of H1 and H2

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 H1, indexing the rows, and H2, indexing the columns
- hierarchy\_small: A data frame carrying the information of ranked similarity between the signatures in H2 with the signatures in H1
- hierarchy\_big: A data frame carrying the information of ranked similarity between the signatures in H1 with the signatures in H2

## See Also

[cosineDist](#)

## Examples

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

---

compare_sets	<i>Compare two sets of signatures by cosine distance</i>
--------------	--

---

## Description

Compare two sets of signatures, stored in numerical data frames  $W1$  and  $W2$ , by computing the column-wise cosine distance

## Usage

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

## Arguments

in\_df\_small, in\_df\_big

Numerical data frames  $W1$  and  $W2$ , ideally the bigger one first, both with  $n$  rows and 11 and 12 columns,  $n$  being the number of features and 11 and 12 being the respective numbers of signatures of  $W1$  and  $W2$

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  $W1$ , indexing the rows, and  $W2$ , indexing the columns
- `hierarchy_small`: A data frame carrying the information of ranked similarity between the signatures in  $W2$  with the signatures in  $W1$
- `hierarchy_big`: A data frame carrying the information of ranked similarity between the signatures in  $W1$  with the signatures in  $W2$

## See Also

[cosineDist](#)

## Examples

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

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

## Arguments

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

## Value

The comparison matrix of cosine similarities.

## See Also

`plot_strata`  
`make_comparison_matrix`

## Examples

NULL

---

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

```
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

```
NULL
```

---

complex\_heatmap\_exposures

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

---

## Description

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

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

## 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 <a href="#">dist</a> . 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 <code>in_subgroups_df</code>
in_subgroup_colour_column	Indicates the name of the column in which the colour information for subgroups is encoded in <code>in_subgroups_df</code> . If NULL, a rainbow palette is used instead.
in_palette	Palette with colours for the heatmap. Default is <code>colorRamp2(c(0, 0.2, 0.4, 0.6), c('white', 'yellow', 'orange', 'red'))</code>
in_cutoff	A numeric value less than 1. Signatures from within $W$ with an overall exposure less than <code>in_cutoff</code> 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

## 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

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

## Value

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

## Examples

`NULL`

---

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 <a href="#">compare_to_catalogues</a>
-----------	---

## Value

A dataframe containing statistical measures, prepared for bar plot

## Examples

```
NULL
```

---

confidence\_indel\_calculation

*Wrapper to compute confidence intervals for SNV and INDEL signatures of a cohort or single-sample*

---

## Description

Wrapper function around [confIntExp](#), which 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 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 data frame 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

```
confidence_indel_only_calculation(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\\_cat](#)

`in_current_snv_df`

A SNV mutational catalog. Mutational catalog can be constructed with [create\\_mutation\\_catalogue](#)

## Value

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

## Examples

```
data("GenomeOfNL_MutCat")
```

---

### confidence\_indel\_only\_calculation

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

---

## Description

Wrapper function around [confIntExp](#), which 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 calculation 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_calculation(in_current_indel_df)
```

## Arguments

`in_current_indel_df`

A INDEL mutational catalog. Mutational catalog can be constructed with [create\\_indel\\_mutation\\_cat](#)

## Details

The function makes use of differnet YAPSA functions. For each of the above stated cutoff vectors a per PID decompostion of the SNV and INDEL catalog is calulated respectivly using [LCD\\_complex\\_cutoff\\_perPID](#). In a next step, [variateExp](#) which is a wrapper around [confIntExp](#) to compute confidenceintervals for a cohort is used. A datafame is returend 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 object. First, the p gtable object which can be used for gaphically visualization, and second a datafame containing the corosponding 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	<i>Compute confidence intervals</i>
------------	-------------------------------------

---

## 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 leve (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 <a href="#">variateExpSingle</a> .

**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 it's 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**

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

**Arguments**

<code>x</code>	vector to be rounded
<code>in_interval</code>	Interval

**Value**

The adapted form of the input vector `x`.

**Examples**

NULL

---

cosineDist*Compute the cosine distance of two vectors*

---

**Description**

Compute the cosine distance of two vectors

**Usage**

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**

```
## 1. Orthogonal vectors:
cosineDist(c(1,0),c(0,1))
## 2. Non-orthogonal vectors:
cosineDist(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**

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

```
## 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 constucted from a vcf-file file the function `create_indel_mutation_catalogue_from_df` creates a mutational catalog  $V$  by sequentially applying the `attribute_sequence_context_indel`, `attribute_sequence_context_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

<code>in_dat</code>	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 user defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.
<code>in_signature_df</code>	A numeric data frame $W$ with $n$ rows and 1 columns, $n$ being the number of features and 1 being the number of signatures. Data frame containing INDEL signatures which should be used to create the mutational catalogue $V$ .
<code>in_REF.field</code>	String indicating which column of <code>in_dat</code> carries the reference base if dealing with data frames
<code>in_ALT.field</code>	String indicating which column of <code>in_dat</code> carries the variant base if dealing with data frames
<code>in_verbose</code>	Verbose if <code>in_verbose=1</code>

**Value**

A dataframe in the format of a mutational catalog  $V$ , which can be used for [LCD](#) analysis

**Examples**

```
data(sigs_pcawg)
data(GenomeOfNL_raw)
temp_df <- translate_to_hg19(GenomeOfNL_raw[1:200,], "CHROM")
temp_df$PID <- sample(c("PID1", "PID2", "PID3", "PID4", "PID5"), 200, replace=TRUE)
temp <- create_indel_mutation_catalogue_from_df(in_dat = temp_df,
  in_signature_df = PCAWG_SP_ID_sigs_df,
  in_REF.field = "REF",
  in_ALT.field = "ALT",
  in_verbose = FALSE)
dim(temp)
head(temp)
```

**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**

```
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 coloums are those of a standart vcf file, followed by an arbitrary number of customs or user defined columns. One of these can carry a PID (patient or sample identifier) and the subgroup information. Additionally to construct the 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 1 columns,  $n$  being the number of features and 1 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

## Examples

```
data(GenomeOfNL_raw)
data(sigs_pcawg)
GenomeOfNL_context <- attribute_sequence_context_indel(in_dat =
  head(GenomeOfNL_raw))
GenomeOfNL_classified <- attribution_of_indels(GenomeOfNL_context)
GenomeOfNL_mut_cat <- create_indel_mut_cat_from_df(GenomeOfNL_classified,
  in_signatures_df=PCAWG_SP_ID_sigs_df)
```

### create\_mutation\_catalogue\_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,
  this_verbose = 1,
  this_rownames = c(),
  this_adapt_rownames = 1
)
```

## Arguments

<code>this_df</code>	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 user defined columns. One of these can carry a PID (patient or sample identifier) and one can carry subgroup information.
<code>this_refGenome_Seqinfo</code>	A seqInfo object, referring to the reference genome used. Argument passed on to <a href="#">makeGRangesFromDataFrame</a> and thus indirectly to <a href="#">makeGRangesFromDataFrame</a> .
<code>this_seqnames.field</code>	Indicates the name of the column in which the chromosome is encoded
<code>this_start.field</code>	Indicates the name of the column in which the start coordinate is encoded

<code>this_end.field</code>	Indicates the name of the column in which the end coordinate is encoded
<code>this_PID.field</code>	Indicates the name of the column in which the PID (patient or sample identifier) is encoded
<code>this_subgroup.field</code>	Indicates the name of the column in which the subgroup information is encoded
<code>this_refGenome</code>	The reference genome handed over to <code>create_mutation_catalogue_from_VR</code> and indirectly to <code>mutationContext</code> and used to extract the motif context of the variants in <code>in_vr</code> .
<code>this_wordLength</code>	The size of the motifs to be extracted by <code>mutationContext</code>
<code>this_verbose</code>	Verbose if <code>this_verbose=1</code>
<code>this_rownames</code>	Optional parameter to specify rownames of the mutational catalogue V i.e. the names of the features.
<code>this_adapt_rownames</code>	Rownames of the output matrix will be adapted if <code>this_adapt_rownames=1</code>

## 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 (IDs) 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

```
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 user 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 <a href="#">mutationContext</a> and used to extract the motif context of the variants in in_vr.
in_wordLength	The size of the motifs to be extracted by <a href="#">mutationContext</a>
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.

## See Also

[mutationContext](#)  
[motifMatrix](#)

## Examples

```

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 Alexandrov 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@googlemail.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

```
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

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

## Value

A list with entries `category_vector`, and `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

```
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	<i>Derive a signature_indices_df object</i>
-----------------	---

---

## 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	<i>Disambiguate a vector</i>
--------------------	------------------------------

---

### Description

Add numbered suffixes to redundant entries in a vector

### Usage

```
disambiguateVector(in_vector)
```

### Arguments

in_vector	Input vector
-----------	--------------

### Value

The disambiguated vector.

### Examples

```
NULL
```

---

enrichSigs	<i>Compare to background distribution</i>
------------	---

---

### 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

```
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	<i>Data structures used in examples, Indel tests and the Indel signature vignette of the YAPSA package.</i>
--------------------	---

---

## 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

<https://www.ncbi.nlm.nih.gov/pubmed/23945592>

---

exampleYAPSA	<i>Test and example data</i>
--------------	------------------------------

---

## 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](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](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](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.

`lymphoma_Nature2013_COSMIC_cutoff_exposures_df`: Data frame with exposures for testing the plot functions. Data taken 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](ftp://ftp.sanger.ac.uk/pub/cancer/AlexandrovEtAl/somatic_mutation_data/Lymphoma%20B-cell/Lymphoma%20B-cell_clean_somatic_mutations_for_signature_analysis.txt).

`rel_lymphoma_Nature2013_COSMIC_cutoff_exposures_df`: Data frame with normalized or relative exposures for testing the plot functions. Data taken 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.

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

```
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)
```

## Author(s)

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

## References

<https://www.ncbi.nlm.nih.gov/pubmed/23945592>

## Examples

```
data(lymphoma_test)
head(lymphoma_test_df)
dim(lymphoma_test_df)
table(lymphoma_test_df$PID)

data(lymphoma_Nature2013_raw)
head(lymphoma_Nature2013_raw_df)
dim(lymphoma_Nature2013_raw_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**

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

---

exposures_barplot	<i>Wrapper for enhanced_barplot</i>
-------------------	-------------------------------------

---

## Description

Wrapper for enhanced\_barplot

## Usage

```
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

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 identifier) 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_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

**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, 1)
```

**Arguments**

in_KEGG_gene_list	Gene list to extract names from
1	Index of the gene to be extracted

**Value**

The gene name.

**See Also**

[keggGet](#)  
[build\\_gene\\_list\\_for\\_pathway](#)

**Examples**

```
NULL
```

---

find\_affected\_PIDs *Find samples affected*

---

### Description

Find samples affected by SNVs in a certain pathway

### Usage

```
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 varinats 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](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

```
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**

```
data(GenomeOfN1_raw)
head(GenomeOfN1_raw)
dim(GenomeOfN1_raw)
```

---

getSequenceContext	<i>Extracts the sequence context up and downstream of a nucleotide position</i>
--------------------	---

---

**Description**

Extracts the sequence context up and downstream of a nucleotide position

**Usage**

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

**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	<i>Return those PIDs which have an extreme pattern for signature exposure</i>
------------------	---

---

## 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	<i>Cluster the PIDs according to their signature exposures</i>
------------------	--

---

## 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 <a href="#">dist</a> . Can be either of: <code>euclidean</code> , <code>maximum</code> , <code>manhattan</code> , <code>canberra</code> , <code>binary</code> or <code>minkowski</code>
in_subgroup_column	Indicates the name of the column in which the subgroup information is encoded in <code>in_subgroups_df</code>
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 <code>in_cutoff</code> 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 <code>in_filename</code>
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  $\min(||W * H - V||)$  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 1 columns,  $n$  being the number of features and 1 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 1 rows and  $m$  columns, 1 being the number of signatures and  $m$  being the number of samples

**See Also**

[lse1](#)

## Examples

```

## 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 catalog
exposures_df <- YAPSA:::LCD(V_compl_df,W_df)
exposures <- as.matrix(exposures_df)

```

## 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  $\min(\|W * H - V\|)$  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.

`LCD_complex_cutoff_combined` is a wrapper for `LCD_complex_cutoff`, `LCD_complex_cutoff_perPID`, `LCD_complex_cutoff_consensus` AND `LCD_extractCohort_callPerPID`.

**Usage**

```

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
)

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 <code>in_cutoff_vector</code> 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 <code>in_cutoff</code> 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 <code>signature_indices_df</code> , 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 <code>in_sig_ind_df</code> . 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 <a href="#">LCD_extractCohort_callPerPID</a> , otherwise, no cutoffs are used.
in_cohort_LCDlist	Optional, if not provided, the cohort-wide exposures are recalculated by calling <a href="#">LCD_complex_cutoff</a>
in_perPID_LCDlist	Optional, if not provided, the per sample exposures are recalculated by calling <a href="#">LCD_complex_cutoff_perPID</a>
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 scalar 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 scalar 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](#)

[lse1](#)

## Examples

`NULL`

---

LCD\_SMC

*CD stratification analysis*

---

## Description

CD stratification analysis

## Usage

`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 1 columns,  $n$  being the number of features and 1 being the number of signatures

`in_F_df`

Default `NULL`

## Value

Returns a list with all exposures and the stratified ones

---

logLikelihood	<i>Compute a loglikelihood ratio test</i>
---------------	---

---

## Description

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

## Usage

```
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 <a href="#">computeLogLik</a> , 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

```
library(BSgenome.Hsapiens.UCSC.hg19)
data(lymphoma_test)
data(sig)
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

```
data(lymphomaNature2013_mutCat_df)
```

### Value

A data fame 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](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 <a href="#">makeGRangesFromDataFrame</a>
in_seqinfo	A seqInfo object, referring to the reference genome used. Argument passed on to <a href="#">makeGRangesFromDataFrame</a>
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

```
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

NULL

---

### make\_comparison\_matrix

*Compute a similarity matrix for different strata*

---

## 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

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

## Arguments

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

**Value**

The comparison matrix of cosine similarities.

**See Also**

[compare\\_SMCs](#)

**Examples**

```
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 <code>in_signatures_ind_df</code> 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

```
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

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

**Value**

subgroups\_df: A data frame carrying the subgroup and rank information.

**See Also**

[aggregate](#)

**Examples**

```
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 <-
  lymphoma_Nature2013_COSMIC_cutoff_exposures_df[,choice_ind]
make_subgroups_df(lymphoma_test_df,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	<i>Merge exposure data frames</i>
-----------------	-----------------------------------

---

### 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 W in which the columns represent the signatures.

### Value

A data frame with the merged exposures.

### Examples

```
NULL
```

---

MutCat_indel_df	<i>Example mutational catalog for the Indel vignette</i>
-----------------	--

---

### 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 fot they biological relevance. Mutational catalog was created with `create_indel_mutation_catalogue_from_df` function.

### Usage

```
data(GenomeOfNl_MutCat)
```

### Value

A data fame 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](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](#)

**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(1,2,3,0,5,2,3,4,0,6,0,0,0,0,0,4,5,6,0,7),
                               ncol=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(1,2,3,0,5,2,3,4,0,6,0,0,0,0,0,4,5,6,0,7),
                               ncol=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(1,2,3,0,5,2,3,4,0,6,0,0,0,0,0,4,5,6,0,7),
                               ncol=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(1,2,3,0,5,2,3,4,0,6,0,0,0,0,0,4,5,6,0,7),
                               ncol=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

```
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

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

## 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

```
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 <a href="#">facet_grid</a>
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. <a href="#">theme_grey</a>

## 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 [variate-Exp](#).

**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**

```
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**

NULL

---

plot_exposures	<i>Plot the exposures of a cohort</i>
----------------	---------------------------------------

---

**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 <code>in_subgroups_df</code> 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)
```

plot\_SMC

*Plot results of the Stratification of a Mutational Catalogue***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,
  output_path,
  decomposition_method,
  number_of_sigs,
  name_list,
  exposures_strata_list,
  this_signatures_ind_df,
  this_subgroups_df,
  in_strata_order_ind,
  exposures_both_rel_df_list,
  cohort_method_flag,
  fig_width = 1200,
  fig_height = 900,
  fig_type = "png",
  in_label_orientation = "turn",
  this_sum_ind = NULL
)
```

**Arguments**

number_of_strata	Number of strata as deduced from <code>link{SMC}</code>
output_path	Path to file where the results are going to be stored. If <code>NULL</code> , 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 contracted strata.
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
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 s strata specific cohortwide (i.e. averaged over cohort) normalized
  exposures
cohort_method_flag
  Either or several of c("all_PIDs", "cohort", "norm_PIDs"), representing alter-
  native 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
  png or 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

```
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

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

### Arguments

in_strata_list	Data structure created by <code>make_strata_df</code> or <code>make_catalogue_strata_df</code> 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**

NULL

---

read\_entry

*Read a single vcf-like file into a single data frame*

---

**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**

```
read_entry(
  current_ind,
  in_list,
  header = TRUE,
  in_header = NULL,
  variant_type = "SNV",
  delete.char = NULL,
  ...
)

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

**Arguments**

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

**Examples**

NULL

NULL

---

`relateSigs`

*Make unique assignments between sets of signatures*

---

**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	<i>Create a data frame with default values</i>
-----------	--

---

## Description

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	<i>Round to a defined precision</i>
-----------------	-------------------------------------

---

## 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 addition 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

```
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"
)
```

## 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](#)

### Usage

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

### Arguments

<code>in_stratification_lists_list</code>	List of lists with entries from different (orthogonal) stratification axes or SMCs
<code>output_path</code>	Path to directory where the results, especially the figure produced by <a href="#">corrplot</a> is going to be stored.
<code>in_nrect</code>	Number of clusters in the clustering procedure provided by <a href="#">corrplot</a>
<code>in_attribute</code>	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

NULL

---

run\_comparison\_general

*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. Function similar to [compare\\_SMCs](#), but without calling [plot\\_strata](#). First calls

- [make\\_strata\\_df](#), then
- [make\\_comparison\\_matrix](#)

## 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 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**

```
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 triplets
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 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

```
run_kmer_frequency_normalization(
  in_ref_genome_fasta,
  in_target_capture_bed,
  in_word_length,
  project_folder,
  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 triplets 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.
- in\_verbose Verbose if in\_verbose=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
)
```

## 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 <a href="#">plot_strata</a> is going to be stored.
in_attribute	Additional string for the file name where the figure produced by <a href="#">plot_strata</a> is going to be stored.
in_remove_signature_ind	Omit one of the signatures in <code>in_signatures_ind_df</code> 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 identifier) and one must be the category used for stratification.
this_signatures_df	A numeric data frame with n rows and 1 columns, n being the number of features and 1 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 identifier) 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 triplets 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 <a href="#">plot_SMC</a> 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 <code>in_all_exposures_df</code> . This is equivalent to forcing the <a href="#">LCD_SMC</a> 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  $H_i$ , all are numerical data frames with  $l$  rows and  $m$  columns,  $l$  being the number of signatures and  $m$  being the number of samples
- `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.

### See Also

[create\\_mutation\\_catalogue\\_from\\_df](#)  
[normalizeMotifs\\_otherRownames](#)  
[plot\\_SMC](#)

### Examples

```
library(BSgenome.Hsapiens.UCSC.hg19)
data(sig)
data(lymphoma_test)
data(lymphoma_cohort_LCD_results)
strata_list <-
  cut_breaks_as_intervals(lymphoma_test_df$random_norm,
                         in_outlier_cutoffs=c(-4,4),
                         in_cutoff_ranges_list=list(c(-2.5,-1.5),
                                                    c(0.5,1.5)),
                         in_labels=c("small","intermediate","big"))
lymphoma_test_df$random_cat <- strata_list$category_vector
choice_ind <- (names(lymphoma_Nature2013_COSMIC_cutoff_exposures_df)
                %in% unique(lymphoma_test_df$PID))
lymphoma_test_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

```
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

```

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"))

```

---

sig	<i>Data for mutational signatures</i>
-----	---------------------------------------

---

### Description

The numerical data of the mutational signatures published initially by Alexandrov et al. (Nature 2013) and Alexandrov et al., (BioRxiv 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> 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

```
data(sigs)
```

## Author(s)

Daniel Huebschmann <huebschmann.daniel@googlemail.com>

## Source

AlexInitial: <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)

sigs\_pcawg

*Data for PCAWG SNV signatures (COSMIC v3), including artifacts*  
*PCAWG\_SP\_SBS\_sigs\_Artif\_df: Data frame of the signatures published by Alexandrov et al. (Biorxiv 2013) which were decomposed with the method SigProfiler. SNV signatures are labeled with SBS, single base signature. There are 67 signatures which constitute the columns, 47 of which were validated by a bayesian NFM method, SignatureAnalyzer. Validated signatures are SBS1-SBS26,SBS28-SBS42 and SBS44. SBS7 is split up into 7 a/b/c and d. SBS10 and SBS17 are both split up into a and b. Resulting in a 47 validated signatures. Please note, unlike the paper by Alexandrov et al. (Biorxiv 2018) the data sets do not contain a SBS84 and SBS85 as not all were available to perform supervised signature analysis. In total there are 96 different features and therefore 96 rows when dealing with a trinucleotide context.*

## 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 Signatures 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 described and thus is not part of this data set. In total 83 features are described. The categorization consideres the size of the insertion and delition, the motif, and the sequence context. Hereby the number of repetition or patal 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-Saile <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)

---

### Description

SMC takes a given collection of stratified mutational catalogues  $V_i$ , 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 $V_i$ (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 <a href="#">run_SMC</a> .
this_signatures_df	A numeric data frame $W$ in 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 1 rows and $m$ columns, 1 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 identifier) 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 1 rows and  $m$  columns, 1 being the number of signatures and  $m$  being the number of samples
- **exposures\_both\_rel\_df\_list**: A list of  $s$  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	<i>Run SMC at a per sample level</i>
------------	--------------------------------------

---

## 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\$signatures) and meta information about the signatures (in_LCDlist\$out_sig_ind_df).
in_subgroups_df	Data frame with subgroup information about the PIDs in the above mentioned cohort.
in_save_plot	Boolean flag to indicate whether per-PID plots should be saved.
in_save_dir	If per-PID plots are to be saved, this is the path where to save them.
in_save_name	Suffix to be appended to the sample name to generate the name of the saved per-PID plots.
in_verbose_flag	Whether to run verbose (1) or not (0).
...	Data passed on to <a href="#">run_SMC</a> .

## Value

A list of lists. The top level is a named per-PID list, each entry is of type SMCList (cf. [run\\_SMC](#)).

## Examples

NULL

---

split\_exposures\_by\_subgroups  
*Split an exposures data frame 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

```
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
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

---

stat\_plot\_subgroups *Plot averaged signature exposures per subgroup*

---

## 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
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	<i>Apply statistical tests to a stratification (SMC)</i>
---------------	--

---

## 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  $H_i$ , all are numerical data frames with  $1$  rows and  $m$  columns,  $1$  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

```
NULL
```

---

stat\_test\_subgroups     *Test for differences in average signature exposures between subgroups*

---

## Description

Apply Kruskal-Wallis tests to detect differences in the signature exposures between different subgroups. Uses [split\\_exposures\\_by\\_subgroups](#). Algorithm analogous to [stat\\_test\\_SMC](#).

## Usage

```
stat_test_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  
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)

**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**

```
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**

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

```
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)
```

targetCapture\_cor\_factors

*Correction factors for different target capture kits*

## 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>

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 <a href="#">confIntExp</a> if NULL assumed to be normal distribution.

**Value**

Returns a data frame

**Examples**

NULL

---

**test\_exposureAffected** *Test significance of association*

---

**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 <a href="#">find_affected_PIDs</a>
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

**Examples**

NULL

---

**transform\_rownames\_R\_to\_MATLAB**

*Change rownames from one naming convention to another*

---

**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 pacakge 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 pacakge.

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 pacakge.

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 pacakge.

**Usage**

```
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**

<code>in_rownames</code>	Character vector of input rownames
<code>wordLength</code>	Size of the considered motif context

**Value**

A character vector of the translated rownames.

**Examples**

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

```
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

```
test_df <- data.frame(CHROM=c(1,2,23,24),POS=c(100,120000000,300000,25000),
                      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(100,120000000,300000,25000),
                      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
```

---

**trellis\_rainfall\_plot** *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.
in_exposures_df	Input numerical data frame of the exposures computed for the cohort to be analyzed.
in_sigLevel	Significance level, parameter passed to <a href="#">confIntExp</a> .
in_delta	Inflation parameter for the alternative model, parameter passed on to <a href="#">confIntExp</a>
in_pdf	Probability distribution function, parameter passed on to <a href="#">confIntExp</a> , if NULL assumed to be normal distribution.

**Value**

A melted data frame.

**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$matrix
lymphoma_PIDs <- colnames(lymphoma_catalogue_df)
data("lymphoma_cohort_LCD_results")
lymphoma_exposures_df <-
  lymphoma_Nature2013_COSMIC_cutoff_exposures_df[,lymphoma_PIDs]
lymphoma_sigs <- rownames(lymphoma_exposures_df)
lymphoma_sig_df <- AlexCosmicValid_sig_df[,lymphoma_sigs]
lymphoma_complete_df <- variateExp(in_catalogue_df = lymphoma_catalogue_df,
                                      in_sig_df = lymphoma_sig_df,
                                      in_exposures_df = lymphoma_exposures_df,
                                      in_sigLevel = 0.025, in_delta = 0.4)
head(lymphoma_complete_df)
lymphoma_complete_df$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"),
        strip.background = element_rect(colour = "black"),
        legend.position = "none") +
  scale_fill_manual(values = sig_colour_vector)

```

**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 <a href="#">logLikelihood</a> and later to <a href="#">computeLogLik</a>
verbose	Verbose if in_verbose=1

**Value**

Returns a list

**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]
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])
```

---

YAPSA

*Generate R documentation from inline comments.*

---

## 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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