

Package ‘musicatk’

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Type Package

Title Mutational Signature Comprehensive Analysis Toolkit

Version 1.15.1

Description Mutational signatures are carcinogenic exposures or aberrant cellular processes that can cause alterations to the genome. We created musicatk (MUtational SIgnature Comprehensive Analysis ToolKit) to address shortcomings in versatility and ease of use in other pre-existing computational tools. Although many different types of mutational data have been generated, current software packages do not have a flexible framework to allow users to mix and match different types of mutations in the mutational signature inference process. Musicatk enables users to count and combine multiple mutation types, including SBS, DBS, and indels. Musicatk calculates replication strand, transcription strand and combinations of these features along with discovery from unique and proprietary genomic feature associated with any mutation type. Musicatk also implements several methods for discovery of new signatures as well as methods to infer exposure given an existing set of signatures. Musicatk provides functions for visualization and downstream exploratory analysis including the ability to compare signatures between cohorts and find matching signatures in COSMIC V2 or COSMIC V3.

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BugReports <https://github.com/campbio/musicatk/issues>

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<code>.jsd</code>	<i>Calculates 1 - Jensen-Shannon Divergences between all pairs of columns between two matrices</i>
-------------------	--

Description

Calculates 1 - Jensen-Shannon Divergences between all pairs of columns between two matrices

Usage

```
.jsd(p, q, epsilon = 1e-07)
```

Arguments

<code>p</code>	First matrix
<code>q</code>	Second matrix
<code>epsilon</code>	Number to add to all probabilities. Default 0.0000001.

Value

Returns matrix of 1 - Jensen-Shannon Divergences

<code>add_flank_to_variants</code>	<i>Uses a genome object to find context and add it to the variant table</i>
------------------------------------	---

Description

Uses a genome object to find context and add it to the variant table

Usage

```
add_flank_to_variants(
  musica,
  g,
  flank_start,
  flank_end,
  build_table = TRUE,
  overwrite = FALSE
)
```

Arguments

musica	Input samples
g	A BSgenome object indicating which genome reference the variants and their coordinates were derived from.
flank_start	Start of flank area to add, can be positive or negative
flank_end	End of flank area to add, can be positive or negative
build_table	Automatically build a table using the annotation and add
overwrite	Overwrite existing count table

Value

None it to the musica

Examples

```
data(musica_sbs96_tiny)
g <- select_genome("19")
add_flank_to_variants(musica_sbs96_tiny, g, 1, 2)
add_flank_to_variants(musica_sbs96_tiny, g, -2, -1)
```

add_variant_type	<i>Generates a variant type table</i>
------------------	---------------------------------------

Description

Generates a variant type table

Usage

```
add_variant_type(tab)
```

Arguments

tab	Input variant table
-----	---------------------

Value

Returns the inputted variant table with variant type ("SBS", "DBS", "INS", "DEL") added as an appended "Variant_Type" column

Examples

```
data(musica)
variants <- variants(musica)
musicatk:::add_variant_type(variants)
```

```
annotate_replication_strand
```

Add replication strand annotation to SBS variants based on bedgraph file

Description

Add replication strand annotation to SBS variants based on bedgraph file

Usage

```
annotate_replication_strand(musica, rep_range, build_table = TRUE)
```

Arguments

musica	A musica object.
rep_range	A GRanges object with replication timing as metadata
build_table	Automatically build a table from this annotation

Value

None

Examples

```
data(musica)
data(rep_range)
annotate_replication_strand(musica, rep_range)
```

```
annotate_transcript_strand
```

Add transcript strand annotation to SBS variants (defined in genes only)

Description

Add transcript strand annotation to SBS variants (defined in genes only)

Usage

```
annotate_transcript_strand(musica, genome_build, build_table = TRUE)
```

Arguments

musica	A musica object.
genome_build	Which genome build to use: hg19, hg38, or a custom TxDb object
build_table	Automatically build a table from this annotation

Value

None

Examples

```
data(musica)
annotate_transcript_strand(musica, 19)
```

annotate_variant_length

Adds an annotation to the input musica's variant table with length of each variant

Description

Adds an annotation to the input musica's variant table with length of each variant

Usage

```
annotate_variant_length(musica)
```

Arguments

musica Input samples

Value

None

Examples

```
data(musica)
annotate_variant_length(musica)
musica
```

annotate_variant_type *Annotate variants with variant type ("SBS", "INS", "DEI", "DBS")*

Description

Annotate variants with variant type ("SBS", "INS", "DEI", "DBS")

Usage

```
annotate_variant_type(musica)
```

Arguments

musica A [musica](#) object.

Value

None

Examples

```
data(musica)
annotate_variant_type(musica)
```

auto_predict_grid	<i>Automatic filtering of signatures for exposure prediction gridded across specific annotation</i>
-------------------	---

Description

Automatic filtering of signatures for exposure prediction gridded across specific annotation

Usage

```
auto_predict_grid(
  musica,
  table_name,
  signature_res,
  algorithm,
  sample_annotation = NULL,
  min_exists = 0.05,
  proportion_samples = 0.25,
  rare_exposure = 0.4,
  verbose = TRUE,
  combine_res = TRUE
)
```

Arguments

musica	Input samples to predict signature weights
table_name	Name of table used for posterior prediction (e.g. SBS96)
signature_res	Signatures to automatically subset from for prediction
algorithm	Algorithm to use for prediction. Choose from "lda_posterior", and decompTumor2Sig
sample_annotation	Annotation to grid across, if none given, prediction subsetting on all samples together
min_exists	Threshold to consider a signature active in a sample
proportion_samples	Threshold of samples to consider a signature active in the cohort
rare_exposure	A sample will be considered active in the cohort if at least one sample has more than this threshold proportion
verbose	Print current annotation value being predicted on
combine_res	Automatically combines a list of annotation results into a single result object with zero exposure values for signatures not found in a given annotation's set of samples

Value

A list of results, one per unique annotation value, if no annotation value is given, returns a single result for all samples, or combines into a single result if `combines_res = TRUE`

Examples

```
data(musica_annot)
data(cosmic_v2_sigs)
auto_predict_grid(musica = musica_annot, table_name = "SBS96",
signature_res = cosmic_v2_sigs, algorithm = "lda",
sample_annotation = "Tumor_Subtypes")
auto_predict_grid(musica_annot, "SBS96", cosmic_v2_sigs, "lda")
```

auto_subset_sigs	<i>Automatic filtering of inactive signatures</i>
------------------	---

Description

Automatic filtering of inactive signatures

Usage

```
auto_subset_sigs(
  musica,
  table_name,
  signature_res,
  algorithm,
  min_exists = 0.05,
  proportion_samples = 0.25,
  rare_exposure = 0.4
)
```

Arguments

<code>musica</code>	A musica object.
<code>table_name</code>	Name of table used for posterior prediction (e.g. SBS96)
<code>signature_res</code>	Signatures to automatically subset from for prediction
<code>algorithm</code>	Algorithm to use for prediction. Choose from "lda_posterior" and <code>decompTumor2Sig</code>
<code>min_exists</code>	Threshold to consider a signature active in a sample
<code>proportion_samples</code>	Threshold of samples to consider a signature active in the cohort
<code>rare_exposure</code>	A sample will be considered active in the cohort if at least one sample has more than this threshold proportion

Value

A result object containing automatically subset signatures and corresponding sample weights

build_custom_table	<i>Builds a custom table from specified user variants</i>
--------------------	---

Description

Builds a custom table from specified user variants

Usage

```
build_custom_table(
  musica,
  variant_annotation,
  name,
  description = character(),
  data_factor = NA,
  annotation_df = NULL,
  features = NULL,
  type = NULL,
  color_variable = NULL,
  color_mapping = NULL,
  return_instead = FALSE,
  overwrite = FALSE
)
```

Arguments

musica	A musica object.
variant_annotation	User column to use for building table
name	Table name to refer to (must be unique)
description	Optional description of the table content
data_factor	Full set of table values, in case some are missing from the data. If NA, a superset of all available unique data values will be used
annotation_df	A data.frame of annotations to use for plotting
features	A data.frame of the input data from which the count table will be built
type	The type of data/mutation in each feature as an Rle object
color_variable	The name of the column of annotation_df used for the coloring in plots
color_mapping	The mapping from the values in the selected color_variable column to color values for plotting
return_instead	Instead of adding to musica object, return the created table
overwrite	Overwrite existing count table

Value

If return_instead = TRUE then the created table object is returned, otherwise the table object is automatically added to the musica's count_tables list and nothing is returned

Examples

```

data(musica)
annotate_transcript_strand(musica, "19", build_table = FALSE)
build_custom_table(musica, "Transcript_Strand", "Transcript_Strand",
data_factor = factor(c("T", "U")))

```

build_standard_table *Builds count tables using various mutation type schemas*

Description

Generates count tables for different mutation type schemas which can be used as input to the mutational signature discovery or prediction functions. "SBS96" generates a table for single base substitutions following the standard 96 mutation types derived from the trinucleotide context. "SBS192" is the 96 mutation type schema with the addition of transcriptional strand or replication strand information added to each base. "DBS" generates a table for the double base substitution schema used in COSMIC V3. "Indel" generates a table for insertions and deletions following the schema used in COSMIC V3.

Usage

```

build_standard_table(
  musica,
  g,
  table_name,
  strand_type = NULL,
  overwrite = FALSE,
  verbose = FALSE
)

```

Arguments

musica	A musica object.
g	A BSgenome object indicating which genome reference the variants and their coordinates were derived from.
table_name	Name of standard table to build. One of "SBS96", "SBS192", "DBS", or "Indel".
strand_type	Strand type to use in SBS192 schema. One of "Transcript_Strand" or "Replication_Strand". Only used if table_name = SBS192.
overwrite	If TRUE, any existing count table with the same name will be overwritten. If FALSE, then an error will be thrown if a table with the same name exists within the musica object.
verbose	Show progress bar for processed samples

Value

No object will be returned. The count tables will be automatically added to the musica object.

Examples

```

g <- select_genome("19")

data(musica)
build_standard_table(musica, g, "SBS96", overwrite = TRUE)

data(musica)
annotate_transcript_strand(musica, "19")
build_standard_table(musica, g, "SBS192", "Transcript_Strand")

data(musica)
data(rep_range)
annotate_replication_strand(musica, rep_range)
build_standard_table(musica, g, "SBS192", "Replication_Strand")

data(dbs_musica)
build_standard_table(dbs_musica, g, "DBS", overwrite = TRUE)

data(indel_musica)
build_standard_table(indel_musica, g, table_name = "INDEL")

```

built_tables	<i>Retrieve the names of count_tables from a musica or musica_result object</i>
--------------	---

Description

The count_tables contains standard and/or custom count tables created from variants

Usage

```

built_tables(object)

## S4 method for signature 'musica'
built_tables(object)

## S4 method for signature 'musica_result'
built_tables(object)

```

Arguments

object A [musica](#) object generated by the [create_musica](#) function or a [musica_result](#) object generated by a mutational discovery or prediction tool.

Value

The names of created count_tables

Examples

```

data(res)
built_tables(res)

```

cluster_exposure *Perform clustering analysis from a musica result object*

Description

Proportional sample exposures will be used as input to perform clustering.

Usage

```
cluster_exposure(
  result,
  nclust,
  proportional = TRUE,
  method = "kmeans",
  dis.method = "euclidean",
  hc.method = "ward.D",
  clara.samples = 5,
  iter.max = 10,
  tol = 1e-15
)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
nclust	Pre-defined number of clusters.
proportional	Logical, indicating if proportional exposure (default) will be used for clustering.
method	Clustering algorithms. Options are "kmeans" (K-means), "hkmeans" (hybrid of hierarchical K-means), "hclust" (hierarchical clustering), "pam" (PAM), and "clara" (Clara).
dis.method	Methods to calculate dissimilarity matrix. Options are "euclidean" (default), "manhattan", "jaccard", "cosine", and "canberra".
hc.method	Methods to perform hierarchical clustering. Options are "ward.D" (default), "ward.D2", "single", "complete", "average", "mcquitty", "median", and "centroid".
clara.samples	Number of samples to be drawn from dataset. Only used when "clara" is selected. Default is 5.
iter.max	Maximum number of iterations for k-means clustering.
tol	Tolerance level for kmeans clustering level iterations

Value

A one-column data frame with sample IDs as row names and cluster number for each sample.

See Also

[kmeans](#)

Examples

```
set.seed(123)
data(res_annot)
clust_out <- cluster_exposure(res_annot, nclust = 2)
```

combine_count_tables *Combines tables into a single table that can be used for discovery/prediction*

Description

Combines tables into a single table that can be used for discovery/prediction

Usage

```
combine_count_tables(
  musica,
  to_comb,
  name,
  description = character(),
  color_variable = character(),
  color_mapping = character(),
  overwrite = FALSE
)
```

Arguments

musica	A musica object.
to_comb	A vector of table names to combine. Each table must already exist within the input musica object
name	Name of table build, must be a new name
description	Description of the new table
color_variable	Annotation column to use for coloring plotted motifs, provided by counts table from input result's musica object
color_mapping	Mapping from color_variable to color names, provided by counts table from input result's musica object
overwrite	Overwrite existing count table

Value

None

Examples

```
g <- select_genome("19")

data(musica)
build_standard_table(musica, g, "SBS96", overwrite = TRUE)

annotate_transcript_strand(musica, "19")
```

```
build_standard_table(musica, g, "SBS192", "Transcript_Strand")  
combine_count_tables(musica, c("SBS96", "SBS192_Trans"), "combo")
```

combine_predict_grid *Combine prediction grid list into a result object. Exposure values are zero for samples in an annotation where that signature was not predicted*

Description

Combine prediction grid list into a result object. Exposure values are zero for samples in an annotation where that signature was not predicted

Usage

```
combine_predict_grid(grid_list, musica, table_name, signature_res)
```

Arguments

grid_list A list of result objects from the prediction grid to combine into a single result
musica A `musica` object.
table_name Table name used for prediction
signature_res Signatures to automatically subset from for prediction

Value

A result object combining all samples and signatures from a prediction grid. Samples have zero exposure value for signatures not found in that annotation type.

Examples

```
data(musica_annot)  
data(cosmic_v2_sigs)  
grid <- auto_predict_grid(musica_annot, "SBS96", cosmic_v2_sigs, "lda",  
"Tumor_Subtypes", combine_res = FALSE)  
combined <- combine_predict_grid(grid, musica_annot, "SBS96", cosmic_v2_sigs)  
plot_exposures(combined, group_by = "annotation",  
annotation="Tumor_Subtypes")
```

compare_cosmic_v2	<i>Compare a result object to COSMIC V2 SBS Signatures (combination whole-exome and whole-genome)</i>
-------------------	---

Description

Compare a result object to COSMIC V2 SBS Signatures (combination whole-exome and whole-genome)

Usage

```
compare_cosmic_v2(
  result,
  threshold = 0.9,
  metric = "cosine",
  result_name = deparse(substitute(result)),
  decimals = 2,
  same_scale = FALSE
)
```

Arguments

result	A musica_result object.
threshold	threshold for similarity
metric	One of "cosine" for cosine similarity or "jsd" for 1 minus the Jensen-Shannon Divergence. Default "cosine".
result_name	title for plot user result signatures
decimals	Specifies rounding for similarity metric displayed. Default 2.
same_scale	If TRUE, the scale of the probability for each signature will be the same. If FALSE, then the scale of the y-axis will be adjusted for each signature. Default TRUE.

Value

Returns the comparisons

Examples

```
data(res)
compare_cosmic_v2(res, threshold = 0.7)
```

compare_cosmic_v3	<i>Compare a result object to COSMIC V3 Signatures; Select exome or genome for SBS and only genome for DBS or Indel classes</i>
-------------------	---

Description

Compare a result object to COSMIC V3 Signatures; Select exome or genome for SBS and only genome for DBS or Indel classes

Usage

```
compare_cosmic_v3(
  result,
  variant_class,
  sample_type,
  metric = "cosine",
  threshold = 0.9,
  result_name = deparse(substitute(result)),
  decimals = 2,
  same_scale = FALSE
)
```

Arguments

result	A musica_result object.
variant_class	Compare to SBS, DBS, or Indel
sample_type	exome (SBS only) or genome
metric	One of "cosine" for cosine similarity or "jsd" for 1 minus the Jensen-Shannon Divergence. Default "cosine".
threshold	threshold for similarity
result_name	title for plot user result signatures
decimals	Specifies rounding for similarity metric displayed. Default 2.
same_scale	If TRUE, the scale of the probability for each signature will be the same. If FALSE, then the scale of the y-axis will be adjusted for each signature. Default TRUE.

Value

Returns the comparisons

Examples

```
data(res)
compare_cosmic_v3(res, "SBS", "genome", threshold = 0.8)
```

compare_results	<i>Compare two result files to find similar signatures</i>
-----------------	--

Description

Compare two result files to find similar signatures

Usage

```
compare_results(
  result,
  other_result,
  threshold = 0.9,
  metric = "cosine",
  result_name = deparse(substitute(result)),
  other_result_name = deparse(substitute(other_result)),
  decimals = 2,
  same_scale = FALSE
)
```

Arguments

result	A musica_result object.
other_result	A second musica_result object.
threshold	threshold for similarity
metric	One of "cosine" for cosine similarity or "jsd" for 1 minus the Jensen-Shannon Divergence. Default "cosine".
result_name	title for plot of first result signatures
other_result_name	title for plot of second result signatures
decimals	Specifies rounding for similarity metric displayed. Default 2.
same_scale	If TRUE, the scale of the probability for each signature will be the same. If FALSE, then the scale of the y-axis will be adjusted for each signature. Default FALSE.

Value

Returns the comparisons

Examples

```
data(res)
compare_results(res, res, threshold = 0.8)
```

cosmic_v2_sigs *COSMIC v2 SBS96 Signatures Result Object*

Description

Data from COSMIC formatted to be used for prediction with individual tumors and cohorts.

Usage

```
data(cosmic_v2_sigs)
```

Format

An object of class `musica_result` See `[predict_exposure()]`.

Source

COSMIC v2, <https://cancer.sanger.ac.uk/cosmic/signatures_v2>

References

Alexandrov, L., Nik-Zainal, S., Wedge, D. et al. (2013) Signatures of mutational processes in human cancer. *Nature* 500, 415–421 ([Nature](<https://www.ncbi.nlm.nih.gov/pubmed/23945592>))

cosmic_v2_subtype_map *Input a cancer subtype to return a list of related COSMIC signatures*

Description

Input a cancer subtype to return a list of related COSMIC signatures

Usage

```
cosmic_v2_subtype_map(tumor_type)
```

Arguments

tumor_type Cancer subtype to view related signatures

Value

Returns signatures related to a partial string match

Examples

```
cosmic_v2_subtype_map ("lung")
```

cosmic_v3_dbs_sigs *COSMIC v3 DBS Genome Signatures Result Object*

Description

Data from COSMIC formatted to be used for prediction with individual tumors and cohorts.

Usage

```
data(cosmic_v3_dbs_sigs)
```

Format

An object of class `musica_result`. See `[predict_exposure()]`.

Source

COSMIC v3, <<https://cancer.sanger.ac.uk/cosmic/signatures>>

References

Alexandrov, L.B., Kim, J., Haradhvala, N.J. et al. (2020) The repertoire of mutational signatures in human cancer. *Nature* 578, 94–101 ([Nature](<https://doi.org/10.1038/s41586-020-1943-3>))

cosmic_v3_indel_sigs *COSMIC v3 Indel Genome Signatures Result Object*

Description

Data from COSMIC formatted to be used for prediction with individual tumors and cohorts.

Usage

```
data(cosmic_v3_indel_sigs)
```

Format

An object of class `musica_result`. See `[predict_exposure()]`.

Source

COSMIC v3, <<https://cancer.sanger.ac.uk/cosmic/signatures>>

References

Alexandrov, L.B., Kim, J., Haradhvala, N.J. et al. (2020) The repertoire of mutational signatures in human cancer. *Nature* 578, 94–101 ([Nature](<https://doi.org/10.1038/s41586-020-1943-3>))

cosmic_v3_sbs_sigs *COSMIC v3 SBS96 Genome Signatures Result Object*

Description

Data from COSMIC formatted to be used for prediction with individual tumors and cohorts.

Usage

```
data(cosmic_v3_sbs_sigs)
```

Format

An object of class `musica_result`. See `[predict_exposure()]`.

Source

COSMIC v3, <<https://cancer.sanger.ac.uk/cosmic/signatures>>

References

Alexandrov, L.B., Kim, J., Haradhvala, N.J. et al. (2020) The repertoire of mutational signatures in human cancer. *Nature* 578, 94–101 ([Nature](<https://doi.org/10.1038/s41586-020-1943-3>))

cosmic_v3_sbs_sigs_exome

COSMIC v3 SBS96 Exome Signatures Result Object

Description

Data from COSMIC formatted to be used for prediction with individual tumors and cohorts.

Usage

```
data(cosmic_v3_sbs_sigs_exome)
```

Format

An object of class `musica_result`. See `[predict_exposure()]`.

Source

COSMIC v3, <<https://cancer.sanger.ac.uk/cosmic/signatures>>

References

Alexandrov, L.B., Kim, J., Haradhvala, N.J. et al. (2020) The repertoire of mutational signatures in human cancer. *Nature* 578, 94–101 ([Nature](<https://doi.org/10.1038/s41586-020-1943-3>))

count_table-class	<i>Object containing the count table matrices, their names and descriptions that we generated by provided and by user functions. These are used to discover and infer signatures and exposures.</i>
-------------------	---

Description

Object containing the count table matrices, their names and descriptions that we generated by provided and by user functions. These are used to discover and infer signatures and exposures.

Slots

name A name that describes the type of table (e.g. "SBS96")

count_table An array of counts with samples as the columns and motifs as the rows

annotation A data.frame of annotations with three columns used for plotting: motif, mutation, and context

features Original features used to generate the count_table

type The mutation type of each feature, in case we need to plot or model they differently

color_variable The variable used for plotting colors, selected from the annotation slot

color_mapping The mapping of the annotations chosen by color_variable to color values for plotting

description A summary table of the result objects in result_list a list of lists. The nested lists created combined (rbind) tables, and the tables at the first list level are modelled independantly. Combined tables must be named. list("tableA", comboTable = list("tableC", "tableD"))

create_dbs78_table	<i>Creates and adds a table for standard doublet base substitution (DBS)</i>
--------------------	--

Description

Creates and adds a table for standard doublet base substitution (DBS)

Usage

```
create_dbs78_table(musica, overwrite = overwrite, verbose)
```

Arguments

musica	A musica object.
overwrite	Overwrite existing count table

Value

Returns the created DBS table object

create_musica	<i>Creates a musica object from a variant table</i>
---------------	---

Description

This function creates a [musica](#) object from a variant table or matrix. The [musica](#) class stores variants information, variant-level annotations, sample-level annotations, and count tables and is used as input to the mutational signature discovery and prediction algorithms. The input variant table or matrix must have columns for chromosome, start position, end position, reference allele, alternate allele, and sample names. The column names in the variant table can be mapped using the `chromosome_col`, `start_col`, `end_col`, `ref_col`, `alt_col`, and `sample_col` parameters.

Usage

```
create_musica(  
  x,  
  genome,  
  check_ref_chromosomes = TRUE,  
  check_ref_bases = TRUE,  
  chromosome_col = "chr",  
  start_col = "start",  
  end_col = "end",  
  ref_col = "ref",  
  alt_col = "alt",  
  sample_col = "sample",  
  extra_fields = NULL,  
  standardize_indels = TRUE,  
  convert_dbs = TRUE,  
  verbose = TRUE  
)
```

Arguments

<code>x</code>	A <code>data.table</code> , <code>matrix</code> , or <code>data.frame</code> that contains columns with the variant information.
<code>genome</code>	A BSgenome object indicating which genome reference the variants and their coordinates were derived from.
<code>check_ref_chromosomes</code>	Whether to perform a check to ensure that the chromosomes in the variant object match the reference chromosomes in the genome object. If there are mismatches, this may cause errors in downstream generation of count tables. If mismatches occur, an attempt to be automatically fix these with the seqlevelsStyle function will be made. Default <code>TRUE</code> .
<code>check_ref_bases</code>	Whether to check if the reference bases in the variant object match the reference bases in the genome object. Default <code>TRUE</code> .
<code>chromosome_col</code>	The name of the column that contains the chromosome reference for each variant. Default <code>"chr"</code> .
<code>start_col</code>	The name of the column that contains the start position for each variant. Default <code>"start"</code> .

end_col	The name of the column that contains the end position for each variant. Default "end".
ref_col	The name of the column that contains the reference base(s) for each variant. Default "ref".
alt_col	The name of the column that contains the alternative base(s) for each variant. Default "alt".
sample_col	The name of the column that contains the sample id for each variant. Default "sample".
extra_fields	Which additional fields to extract and include in the musica object. Default NULL.
standardize_indels	Flag to convert indel style (e.g. 'C > CAT' becomes '- > AT' and 'GCACA > G' becomes 'CACACA > -')
convert_dbs	Flag to convert adjacent SBS into DBS (original SBS are removed)
verbose	Whether to print status messages during error checking. Default TRUE.

Value

Returns a musica object

Examples

```
maf_file <- system.file("extdata", "public_TCGA.LUSC.maf",
  package = "musicatk")
variants <- extract_variants_from_maf_file(maf_file)
g <- select_genome("38")
musica <- create_musica(x = variants, genome = g)
```

create_sbs192_table *Uses a genome object to find context and generate standard SBS192 table using transcript strand*

Description

Uses a genome object to find context and generate standard SBS192 table using transcript strand

Usage

```
create_sbs192_table(musica, g, strand_type, overwrite = FALSE)
```

Arguments

musica	Input samples
g	A BSgenome object indicating which genome reference the variants and their coordinates were derived from.
strand_type	Transcript_Strand or Replication_Strand
overwrite	Overwrite existing count table

Value

Returns the created SBS192 count table object built using either transcript strand or replication strand

create_sbs96_table	<i>Uses a genome object to find context and generate standard SBS96 tables</i>
--------------------	--

Description

Uses a genome object to find context and generate standard SBS96 tables

Usage

```
create_sbs96_table(musica, g, overwrite = FALSE)
```

Arguments

musica	A musica object.
g	A BSgenome object indicating which genome reference the variants and their coordinates were derived from.
overwrite	Overwrite existing count table

Value

Returns the created SBS96 count table object

create_umap	<i>Create a UMAP from a musica result</i>
-------------	---

Description

Proportional sample exposures will be used as input into the [umap](#) function to generate a two dimensional UMAP.

Usage

```
create_umap(result, n_neighbors = 30, min_dist = 0.75, spread = 1)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
n_neighbors	The size of local neighborhood used for views of manifold approximation. Larger values result in more global the manifold, while smaller values result in more local data being preserved. If n_neighbors is larger than the number of samples, then n_neighbors will automatically be set to the number of samples in the musica_result . Default 30.
min_dist	The effective minimum distance between embedded points. Smaller values will result in a more clustered/clumped embedding where nearby points on the manifold are drawn closer together, while larger values will result on a more even dispersal of points. Default 0.2.
spread	The effective scale of embedded points. In combination with 'min_dist', this determines how clustered/clumped the embedded points are. Default 1.

Value

A `musica_result` object with a new UMAP stored in the UMAP slot.

See Also

See `plot_umap` to display the UMAP and `umap` for more information on the individual parameters for generating UMAPs.

Examples

```
data(res_annot)
create_umap(result = res_annot)
```

<code>dbs_musica</code>	<i>dbs_musica</i>
-------------------------	-------------------

Description

A `musica` created for testing that includes DBS variants

Usage

```
data(dbs_musica)
```

Format

An object of class `musica` See `[create_musica()]`.

<code>discover_signatures</code>	<i>Discover mutational signatures</i>
----------------------------------	---------------------------------------

Description

Mutational signatures and exposures will be discovered using methods such as Latent Dirichlet Allocation (`lda`) or Non-Negative Matrix Factorization (`nmf`). These algorithms will deconvolute a matrix of counts for mutation types in each sample to two matrices: 1) a "signature" matrix containing the probability of each mutation type in each sample and 2) an "exposure" matrix containing the estimated counts for each signature in each sample. Before mutational discovery can be performed, variants from samples first need to be stored in a `musica` object using the `create_musica` function and mutation count tables need to be created using functions such as `build_standard_table`.

Usage

```
discover_signatures(
  musica,
  table_name,
  num_signatures,
  algorithm = "lda",
  seed = 1,
  nstart = 10,
  par_cores = 1
)
```

Arguments

musica	A musica object.
table_name	Name of the table to use for signature discovery. Needs to be the same name supplied to the table building functions such as build_standard_table .
num_signatures	Number of signatures to discover.
algorithm	Method to use for mutational signature discovery. One of "lda" or "nmf". Default "lda".
seed	Seed to be used for the random number generators in the signature discovery algorithms. Default 1.
nstart	Number of independent random starts used in the mutational signature algorithms. Default 10.
par_cores	Number of parallel cores to use. Only used if method = "nmf". Default 1.

Value

Returns a A [musica_result](#) object containing signatures and exposures.

Examples

```
data(musica)
g <- select_genome("19")
build_standard_table(musica, g, "SBS96", overwrite = TRUE)
discover_signatures(musica = musica, table_name = "SBS96",
  num_signatures = 3, algorithm = "lda", seed = 12345, nstart = 1)
```

drop_annotation	<i>Drops a column from the variant table that the user no longer needs</i>
-----------------	--

Description

Drops a column from the variant table that the user no longer needs

Usage

```
drop_annotation(musica, column_name)
```

Arguments

musica	A musica object.
column_name	Name of column to drop

Value

None

Examples

```
data(musica)
drop_annotation(musica, "Variant_Type")
```

exposures	<i>Retrieve exposures from a musica_result object</i>
-----------	---

Description

The exposure matrix contains estimated amount of each signature for each sample. Rows correspond to each signature and columns correspond to each sample.

Usage

```
exposures(result)

## S4 method for signature 'musica_result'
exposures(result)

exposures(result) <- value

## S4 replacement method for signature 'musica_result,matrix'
exposures(result) <- value
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
value	A matrix of samples by signature exposures

Value

A matrix of exposures

Examples

```
data(res)
exposures(res)
data(res)
exposures(res) <- matrix()
```

exposure_differential_analysis	<i>Compare exposures of annotated samples</i>
--------------------------------	---

Description

exposure_differential_analysis is used to run differential analysis on the signature exposures of annotated samples within the [musica_result](#) object.

Usage

```

exposure_differential_analysis(
  musica_result,
  annotation,
  method = c("wilcox", "kruskal", "glm.nb"),
  group1 = NULL,
  group2 = NULL,
  ...
)

```

Arguments

musica_result	A musica_result object
annotation	Column in the sample_annotations table of the musica_result object
method	Any method in c("wilcox", "kruskal", "glm.nb") used to perform differential analysis on signature exposures
group1	character vector used in the Wilcox test. Elements in group1 are compared to elements in group2. This is required for annotation with more than 2 levels.
group2	character vector used in the Wilcox test. Elements in group2 are compared to elements in group1. This is required for annotation with more than 2 levels.
...	Additional arguments to be passed to the chosen method

Value

A matrix containing statistics summarizing the analysis dependent on the chosen method

Examples

```

data("res_annot")
exposure_differential_analysis(res_annot, "Tumor_Subtypes", method="wilcox")

```

extract_count_tables *Extract count tables list from a musica object*

Description

Extract count tables list from a musica object

Usage

```
extract_count_tables(musica)
```

Arguments

musica	A musica object.
--------	----------------------------------

Value

List of count tables objects

Examples

```
data(musica)
extract_count_tables(musica)
```

extract_variants	<i>Extract variants from multiple objects</i>
------------------	---

Description

Chooses the correct function to extract variants from input based on the class of the object or the file extension. Different types of objects can be mixed within the list. For example, the list can include VCF files and maf objects. Certain parameters such as `id` and `rename` only apply to VCF objects or files and need to be individually specified for each VCF. Therefore, these parameters should be supplied as a vector that is the same length as the number of inputs. If other types of objects are in the input list, then the value of `id` and `rename` will be ignored for these items.

Usage

```
extract_variants(
  inputs,
  id = NULL,
  rename = NULL,
  sample_field = NULL,
  filename_as_id = FALSE,
  strip_extension = c(".vcf", ".vcf.gz", ".gz"),
  filter = TRUE,
  multiallele = c("expand", "exclude"),
  fix_vcf_errors = TRUE,
  extra_fields = NULL,
  chromosome_col = "chr",
  start_col = "start",
  end_col = "end",
  ref_col = "ref",
  alt_col = "alt",
  sample_col = "sample",
  verbose = TRUE
)
```

Arguments

<code>inputs</code>	A vector or list of objects or file names. Objects can be CollapsedVCF , ExpandedVCF , MAF , an object that inherits from <code>matrix</code> or <code>data.frame</code> , or character strings that denote the path to a vcf or maf file.
<code>id</code>	A character vector the same length as <code>inputs</code> denoting the sample to extract from a vcf. See extract_variants_from_vcf for more details. Only used if the input is a vcf object or file. Default <code>NULL</code> .
<code>rename</code>	A character vector the same length as <code>inputs</code> denoting what the same will be renamed to. See extract_variants_from_vcf for more details. Only used if the input is a vcf object or file. Default <code>NULL</code> .

sample_field	Some algorithms will save the name of the sample in the ##SAMPLE portion of header in the VCF. See extract_variants_from_vcf for more details. Default NULL.
filename_as_id	If set to TRUE, the file name will be used as the sample name. See extract_variants_from_vcf_file for more details. Only used if the input is a vcf file. Default TRUE.
strip_extension	Only used if filename_as_id is set to TRUE. If set to TRUE, the file extension will be stripped from the filename before setting the sample name. See extract_variants_from_vcf_file for more details. Only used if the input is a vcf file. Default c(".vcf", ".vcf.gz", ".gz")
filter	Exclude variants that do not have a PASS in the FILTER column of VCF inputs.
multiallele	Multialleles are when multiple alternative variants are listed in the same row in the vcf. See extract_variants_from_vcf for more details. Only used if the input is a vcf object or file. Default "expand".
fix_vcf_errors	Attempt to automatically fix VCF file formatting errors. See extract_variants_from_vcf_file for more details. Only used if the input is a vcf file. Default TRUE.
extra_fields	Optionally extract additional fields from all input objects. Default NULL.
chromosome_col	The name of the column that contains the chromosome reference for each variant. Only used if the input is a matrix or data.frame. Default "Chromosome".
start_col	The name of the column that contains the start position for each variant. Only used if the input is a matrix or data.frame. Default "Start_Position".
end_col	The name of the column that contains the end position for each variant. Only used if the input is a matrix or data.frame. Default "End_Position".
ref_col	The name of the column that contains the reference base(s) for each variant. Only used if the input is a matrix or data.frame. Default "Tumor_Seq_Allele1".
alt_col	The name of the column that contains the alternative base(s) for each variant. Only used if the input is a matrix or data.frame. Default "Tumor_Seq_Allele2".
sample_col	The name of the column that contains the sample id for each variant. Only used if the input is a matrix or data.frame. Default "sample".
verbose	Show progress of variant extraction. Default TRUE.

Value

Returns a data.table of variants from a vcf

Examples

```
# Get locations of two vcf files and a maf file
luad_vcf_file <- system.file("extdata", "public_LUAD_TCGA-97-7938.vcf",
  package = "musicatk")
lusc_maf_file <- system.file("extdata", "public_TCGA.LUSC.maf",
  package = "musicatk")
melanoma_vcfs <- list.files(system.file("extdata", package = "musicatk"),
  pattern = glob2rx("*SKCM*vcf"), full.names = TRUE)

# Read all files in at once
inputs <- c(luad_vcf_file, melanoma_vcfs, lusc_maf_file)
variants <- extract_variants(inputs = inputs)
table(variants$sample)
```

```
# Run again but renaming samples in first four vcfs
new_name <- c(paste0("Sample", 1:4), NA)
variants <- extract_variants(inputs = inputs, rename = new_name)
table(variants$sample)
```

extract_variants_from_maf

Extract variants from a maf object

Description

Add description

Usage

```
extract_variants_from_maf(maf, extra_fields = NULL)
```

Arguments

maf MAF object loaded by read.maf() from the 'maftools' package
 extra_fields Optionally extract additional columns from the maf object. Default NULL.

Value

Returns a data.table of variants from a maf which can be used to create a musica object.

Examples

```
maf_file <- system.file("extdata", "public_TCGA.LUSC.maf",
  package = "musicatk")
library(maftools)
maf <- read.maf(maf_file)
variants <- extract_variants_from_maf(maf = maf)
```

extract_variants_from_maf_file

Extracts variants from a maf file

Description

Add Description - Aaron

Usage

```
extract_variants_from_maf_file(maf_file, extra_fields = NULL)
```

Arguments

maf_file Location of maf file
 extra_fields Optionally extract additional columns from the object. Default NULL.

Value

Returns a data.table of variants from a maf

Examples

```
maf_file <- system.file("extdata", "public_TCGA.LUSC.maf",
  package = "musicatk")
maf <- extract_variants_from_maf_file(maf_file = maf_file)
```

extract_variants_from_matrix

Extract variants from matrix or data.frame like objects

Description

Add Description

Usage

```
extract_variants_from_matrix(
  mat,
  chromosome_col = "Chromosome",
  start_col = "Start_Position",
  end_col = "End_Position",
  ref_col = "Tumor_Seq_Allele1",
  alt_col = "Tumor_Seq_Allele2",
  sample_col = "Tumor_Sample_Barcode",
  extra_fields = NULL
)
```

Arguments

mat	An object that inherits from classes "matrix" or "data.frame" Examples include a matrix, data.frame, or data.table.
chromosome_col	The name of the column that contains the chromosome reference for each variant. Default "Chromosome".
start_col	The name of the column that contains the start position for each variant. Default "Start_Position".
end_col	The name of the column that contains the end position for each variant. Default "End_Position".
ref_col	The name of the column that contains the reference base(s) for each variant. Default "Tumor_Seq_Allele1".
alt_col	The name of the column that contains the alternative base(s) for each variant. Default "Tumor_Seq_Allele2".
sample_col	The name of the column that contains the sample id for each variant. Default "Tumor_Sample_Barcode".
extra_fields	Optionally extract additional columns from the object. Default NULL.

Value

Returns a data.table of variants from a maf which can be used to create a musica object.

Examples

```
maf_file <- system.file("extdata", "public_TCGA.LUSC.maf",
  package = "musicatk")
library(maftools)
maf <- read.maf(maf_file)
variants <- extract_variants_from_maf(maf = maf)
variants <- extract_variants_from_matrix(mat = variants,
  chromosome_col = "chr", start_col = "start", end_col = "end",
  ref_col = "ref", alt_col = "alt", sample_col = "sample")
```

extract_variants_from_vcf

Extracts variants from a VariantAnnotation VCF object

Description

Aaron - Need to describe difference between ID, and name in the header, and rename in terms of naming the sample. Need to describe differences in multiallelic choices. Also need to describe the automatic error fixing

Usage

```
extract_variants_from_vcf(
  vcf,
  id = NULL,
  rename = NULL,
  sample_field = NULL,
  filter = TRUE,
  multiallele = c("expand", "exclude"),
  extra_fields = NULL
)
```

Arguments

vcf	Location of vcf file
id	ID of the sample to select from VCF. If NULL, then the first sample will be selected. Default NULL.
rename	Rename the sample to this value when extracting variants. If NULL, then the sample will be named according to ID.
sample_field	Some algorithms will save the name of the sample in the ##SAMPLE portion of header in the VCF (e.g. ##SAMPLE=<ID=TUMOR,SampleName=TCGA-01-0001>). If the ID is specified via the id parameter ("TUMOR" in this example), then sample_field can be used to specify the name of the tag ("SampleName" in this example). Default NULL.
filter	Exclude variants that do not have a PASS in the FILTER column of the VCF. Default TRUE.

multiallele	Multialleles are when multiple alternative variants are listed in the same row in the vcf. One of "expand" or "exclude". If "expand" is selected, then each alternate allele will be given their own rows. If "exclude" is selected, then these rows will be removed. Default "expand".
extra_fields	Optionally extract additional fields from the INFO section of the VCF. Default NULL.

Value

Returns a data.table of variants from a vcf

Examples

```
vcf_file <- system.file("extdata", "public_LUAD_TCGA-97-7938.vcf",
  package = "musicatk")

library(VariantAnnotation)
vcf <- readVcf(vcf_file)
variants <- extract_variants_from_vcf(vcf = vcf)
```

extract_variants_from_vcf_file

Extracts variants from a vcf file

Description

Add Description

Usage

```
extract_variants_from_vcf_file(
  vcf_file,
  id = NULL,
  rename = NULL,
  sample_field = NULL,
  filename_as_id = FALSE,
  strip_extension = c(".vcf", ".vcf.gz", ".gz"),
  filter = TRUE,
  multiallele = c("expand", "exclude"),
  extra_fields = NULL,
  fix_vcf_errors = TRUE
)
```

Arguments

vcf_file	Path to the vcf file
id	ID of the sample to select from VCF. If NULL, then the first sample will be selected. Default NULL.
rename	Rename the sample to this value when extracting variants. If NULL, then the sample will be named according to ID.

sample_field	Some algorithms will save the name of the sample in the ##SAMPLE portion of header in the VCF (e.g. ##SAMPLE=<ID=TUMOR,SampleName=TCGA-01-0001>). If the ID is specified via the id parameter ("TUMOR" in this example), then sample_field can be used to specify the name of the tag ("SampleName" in this example). Default NULL.
filename_as_id	If set to TRUE, the file name will be used as the sample name.
strip_extension	Only used if filename_as_id is set to TRUE. If set to TRUE, the file extension will be stripped from the filename before setting the sample name. If a character vector is given, then all the strings in the vector will be removed from the end of the filename before setting the sample name. Default c(".vcf", ".vcf.gz", ".gz")
filter	Exclude variants that do not have a PASS in the FILTER column of the VCF. Default TRUE.
multiallele	Multialleles are when multiple alternative variants are listed in the same row in the vcf. One of "expand" or "exclude". If "expand" is selected, then each alternate allele will be given their own rows. If "exclude" is selected, then these rows will be removed. Default "expand".
extra_fields	Optionally extract additional fields from the INFO section of the VCF. Default NULL.
fix_vcf_errors	Attempt to automatically fix VCF file formatting errors.

Value

Returns a data.table of variants extracted from a vcf

Examples

```
vcf <- system.file("extdata", "public_LUAD_TCGA-97-7938.vcf",
  package = "musicatk")
variants <- extract_variants_from_vcf_file(vcf_file = vcf)
```

generate_result_grid *Generate result_grid from musica based on annotation and range of k*

Description

Generate result_grid from musica based on annotation and range of k

Usage

```
generate_result_grid(
  musica,
  table_name,
  algorithm = "lda",
  annotation = NA,
  k_start,
  k_end,
  n_start = 1,
  seed = NULL,
  par_cores = FALSE,
  verbose = FALSE
)
```

Arguments

musica	A musica object.
table_name	Name of table used for signature discovery
algorithm	Algorithm for signature discovery
annotation	Sample annotation to split results into
k_start	Lower range of number of signatures for discovery
k_end	Upper range of number of signatures for discovery
n_start	Number of times to discover signatures and compare based on posterior loglikelihood
seed	Seed to use for reproducible results, set to null to disable
par_cores	Number of parallel cores to use (NMF only)
verbose	Whether to output loop iterations

Value

A result object containing signatures and sample weights

Examples

```
data(musica_sbs96)
grid <- generate_result_grid(musica_sbs96, "SBS96", "lda", k_start = 2,
k_end = 5)
```

get_musica	<i>Retrieve musica from a musica_result object</i>
------------	--

Description

The [musica](#) musica contains variants, count tables, and sample annotations

Usage

```
get_musica(result)

## S4 method for signature 'musica_result'
get_musica(result)
```

Arguments

result A [musica_result](#) object generated by a mutational discovery or prediction tool.

Value

A [musica](#) musica object

Examples

```
data(res)
get_musica(res)
```

indel_musica	<i>indel_musica</i>
--------------	---------------------

Description

A musica created for testing that includes INDEL variants

Usage

```
data(indel_musica)
```

Format

An object of class musica See [create_musica()].

k_select	<i>Plots for helping decide number of clusters</i>
----------	--

Description

To help decide the number of cluster, three different methods are provided: total within cluster sum of squares, average silhouette coefficient, and gap statistics.

Usage

```
k_select(
  result,
  method = "wss",
  clust.method = "kmeans",
  n = 10,
  proportional = TRUE
)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
method	A single character string indicating which statistic to use for plot. Options are "wss" (total within cluster sum of squares), "silhouette" (average silhouette coefficient), and "gap_stat" (gap statistic). Default is "wss".
clust.method	A character string indicating clustering method. Options are "kmeans" (default), "hclust" (hierarchical clustering), "hkmeans", "pam", and "clara".
n	An integer indicating maximum number of clusters to test. Default is 10.
proportional	Logical, indicating if proportional exposure (default) will be used for clustering.

Value

A ggplot object.

See Also[fviz_nbclust](#)**Examples**

```

data(res_annot)
set.seed(123)
#Make an elbow plot
k_select(res_annot, method = "wss", n = 6)
#Plot average silhouette coefficient against number of clusters
k_select(res_annot, method = "silhouette", n = 6)
#Plot gap statistics against number of clusters
k_select(res_annot, method = "gap_stat", n = 6)

```

musica

musica

Description

A musica created for testing that includes SBS variants

Usage

```
data(musica)
```

Format

An object of class musica See [create_musica()].

musica-class

The primary object that contains variants, count_tables, and samples annotations

Description

The primary object that contains variants, count_tables, and samples annotations

Slots

variants data.table of variants

count_tables Summary table with per-sample unnormalized motif counts

sample_annotations Sample-level annotations (e.g. age, sex, primary)

musicatk	<i>Starts the musicatk interactive Shiny app</i>
----------	--

Description

The musicatk Shiny app allows users to perform mutational signature analysis using an interactive graphical user interface (GUI)

Usage

```
musicatk(include_version = TRUE, theme = "yeti")
```

Arguments

include_version	Include the version number in the header. Default TRUE.
theme	The theme to use for the GUI. Default "yeti".

Value

The shiny app will open. No data will be returned.

Examples

```
## Not run:  
# Start the app  
musicatk()  
  
## End(Not run)
```

musica_annot	<i>musica_annot</i>
--------------	---------------------

Description

A musica created for testing that includes SBS variants and sample annotations

Usage

```
data(musica_annot)
```

Format

An object of class musica See [create_musica()].

`musica_result-class` *Object containing deconvolved/predicted signatures, sample weights, and the musica object the result was generated from*

Description

Object containing deconvolved/predicted signatures, sample weights, and the musica object the result was generated from

Slots

`signatures` A matrix of signatures by mutational motifs
`exposures` A matrix of samples by signature weights
`table_name` A character vector of table names used to make the result
`algorithm` Describes how the signatures/weights were generated
`musica` The musica object the results were generated from
`umap` List of umap data.frames for plotting and analysis

`musica_result_grid-class`

Object containing the result objects generated from the combination of annotations and a range of k values

Description

Object containing the result objects generated from the combination of annotations and a range of k values

Slots

`grid_params` The parameters the result grid was created using
`result_list` A list of result objects with different parameters
`grid_table` A summary table of the result objects in `result_list`

`musica_sbs96`

musica_sbs96

Description

A musica created for testing that includes SBS variants and a build counts table for them

Usage

```
data(musica_sbs96)
```

Format

An object of class `musica` See `[build_standard_table()]`.

musica_sbs96_tiny	<i>musica_sbs96_tiny</i>
-------------------	--------------------------

Description

A very small musica created for testing that includes SBS variants and a build counts table for them

Usage

```
data(musica_sbs96_tiny)
```

Format

An object of class musica See [build_standard_table()].

name_signatures	<i>Return sample from musica object</i>
-----------------	---

Description

Return sample from musica object

Usage

```
name_signatures(result, name_vector)
```

Arguments

result	Result object containing signatures and weights
name_vector	Vector of user-defined signature names

Value

Result object with user-defined signatures names

Examples

```
data(res)
name_signatures(res, c("smoking", "apobec", "unknown"))
```

plot_cluster	<i>Visualize clustering results</i>
--------------	-------------------------------------

Description

The clustering results can be visualized on a UMAP panel. Three different types of plots can be generated using this function: cluster-by-signature plot, cluster-by-annotation plot, and a single UMAP plot.

Usage

```
plot_cluster(  
  result,  
  clusters,  
  group = "signature",  
  annotation = NULL,  
  plotly = TRUE  
)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool. A two-dimensional UMAP has to be stored in this object.
clusters	The result generated from <code>cluster_exposure</code> function.
group	A single character string indicating the grouping factor. Possible options are: "signature" (columns are signatures in a grid), "annotation" (columns are sample annotation), and "none" (a single UMAP plot). Default is "signature".
annotation	Column name of annotation.
plotly	If TRUE, the plot will be made interactive using plotly.

Value

Generate a ggplot or plotly object.

See Also

[create_umap](#)

Examples

```
set.seed(123)  
data(res_annot)  
#Get clustering result  
clust_out <- cluster_exposure(result = res_annot, nclust = 2)  
#UMAP  
create_umap(result = res_annot)  
#generate cluster X signature plot  
plot_cluster(result = res_annot, clusters = clust_out, group = "signature")  
#generate cluster X annotation plot  
plot_cluster(result = res_annot, clusters = clust_out, group = "annotation",  
             annotation = "Tumor_Subtypes")
```

```
#generate a single UMAP plot
plot_cluster(result = res_annot, clusters = clust_out, group = "none")
```

plot_differential_analysis

Compare exposures of annotated samples

Description

plot_differential_analysis is used to plot differential analysis created by exposure_differential_analysis.

Usage

```
plot_differential_analysis(analysis, analysis_type, samp_num)
```

Arguments

analysis	Analysis created by exposure_differential_analysis
analysis_type	Currently only "glm" supported
samp_num	Number of samples that went into the analysis

Value

Generates a ggplot object

Examples

```
data("res_annot")
analysis <- exposure_differential_analysis(res_annot, "Tumor_Subtypes",
method="wilcox")
plot_differential_analysis(analysis, "glm", 2)
```

plot_exposures

Display sample exposures with bar, box, or violin plots

Description

The distributions of mutational signatures can be viewed with barplots or box/violin plots. Barplots are most useful for viewing the proportion of signatures within and across samples. The box/violin plots are most useful for viewing the distributions of signatures with respect to sample annotations. Samples can be grouped using the group_by parameter. For barplots, various methods of sorting samples from left to right can be chosen using the sort_samples parameter.

Usage

```
plot_exposures(
  result,
  plot_type = c("bar", "box", "violin"),
  proportional = FALSE,
  group_by = "none",
  color_by = c("signature", "annotation"),
  annotation = NULL,
  num_samples = NULL,
  sort_samples = "total",
  threshold = NULL,
  same_scale = FALSE,
  add_points = FALSE,
  point_size = 2,
  label_x_axis = FALSE,
  legend = TRUE,
  plotly = FALSE
)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
plot_type	One of "bar", "box", or "violin". Default "bar".
proportional	If TRUE, then the exposures will be normalized to between 0 and 1 by dividing by the total number of counts for each sample. Default FALSE.
group_by	Determines how to group samples into the subplots (i.e. facets). One of "none", "signature" or "annotation". If set to "annotation", then a sample annotation must be supplied via the annotation parameter. Default "none".
color_by	Determines how to color the bars or box/violins. One of "signature" or "annotation". If set to "annotation", then a sample annotation must be supplied via the annotation parameter. Default "signature".
annotation	Sample annotation used to group the subplots and/or color the bars, boxes, or violins. Default NULL.
num_samples	The top number of sorted samples to display. If NULL, then all samples will be displayed. If group_by is set, then the top samples will be shown within each group. Default NULL.
sort_samples	This is used to change how samples are sorted in the barplot from left to right. If set to "total", then samples will be sorted from those with the highest number of mutation counts to the lowest (regardless of how the parameter "proportional" is set). If set to "name", then samples are sorted by their name with the mixedsort function. If set to one or more signature names (e.g. "Signature1"), then samples will be sorted from those with the highest level of that signature to the lowest. If multiple signatures are supplied then, samples will be sorted by each signature sequentially. Default "total".
threshold	Exposures less than this threshold will be set to 0. This is most useful when more than one signature is supplied to sort_samples as samples that are set to zero for the first exposure will then be sorted by the levels of the second exposure. Default NULL.
same_scale	If TRUE, then all subplots will have the same scale. Only used when group_by is set. Default FALSE.

add_points	If TRUE, then points for individual sample exposures will be plotted on top of the violin/box plots. Only used when plot_type is set to "violin" or "box". Default TRUE.
point_size	Size of the points to be plotted on top of the violin/box plots. Only used when plot_type is set to "violin" or "box" and add_points is set to TRUE. Default 2.
label_x_axis	If TRUE, x-axis labels will be displayed at the bottom of the plot. Default FALSE.
legend	If TRUE, the legend will be displayed. Default TRUE.
plotly	If TRUE, the the plot will be made interactive using plotly . Default FALSE.

Value

Generates a ggplot or plotly object

Examples

```
data(res_annot)
plot_exposures(res_annot, plot_type = "bar", annotation = "Tumor_Subtypes")
```

plot_heatmap

Plot heatmaps using the exposures matrix

Description

The exposures for different signatures can be visualized using a heatmap with this function. Heatmaps make it easier to visualize the data by representing the magnitude of exposure values as color in 2-dimensions. The variation in color intensity can help see if the exposures are clustered or how they vary over space. Exposures can be normalized by providing the `proportional` argument. Column annotations can also be seen by passing the `col_annot` argument.

Usage

```
plot_heatmap(
  res_annot,
  proportional = FALSE,
  show_column_names = FALSE,
  show_row_names = TRUE,
  scale = TRUE,
  subset_tumor = NULL,
  subset_signatures = NULL,
  annotation = NULL,
  ...
)
```

Arguments

res_annot	A musica_result object generated by a mutational discovery or prediction tool.
proportional	If TRUE, then the exposures will be normalized to between 0 and 1 by dividing by the total number of counts for each sample. Default FALSE.

show_column_names	Boolean check. If True, column names are shown. Otherwise, they aren't. Default FALSE
show_row_names	Boolean check. If True, row names are shown. Otherwise, they aren't. Default FALSE
scale	Boolean check. If True, values are scaled by z-score. Otherwise, they aren't. Default TRUE
subset_tumor	Users can specify certain tumor types on which they want to subset the exposure matrix for plotting the heatmap.
subset_signatures	Users can specify certain signatures on which they want to subset the exposure matrix plotting the heatmap.
annotation	Users have the option of plotting the exposure matrix based on their given annotation like Tumor_Subtypes or age. Error given if the user given annotation doesn't exist in the res_annot annotation object.
...	Ellipsis used for passing any arguments directly to the ComplexHeatmap's heatmap function.

Value

Generates a heatmap for using the exposure matrix.

Examples

```
data(res_annot)
plot_heatmap(res_annot = res_annot, proportional = TRUE, scale = TRUE,
annotation = "Tumor_Subtypes")
```

plot_sample_counts *Plot distribution of sample counts*

Description

Displays the proportion of counts for each mutation type across one or more samples.

Usage

```
plot_sample_counts(
  musica,
  sample_names,
  table_name = NULL,
  text_size = 10,
  show_x_labels = TRUE,
  show_y_labels = TRUE,
  same_scale = TRUE,
  annotation = NULL
)
```

Arguments

musica	A <code>musica</code> object.
sample_names	Names of the samples to plot.
table_name	Name of table used for plotting counts. If NULL, then the first table in the <code>musica</code> object will be used. Default NULL.
text_size	Size of axis text. Default 10.
show_x_labels	If TRUE, the labels for the mutation types on the x-axis will be shown. Default TRUE.
show_y_labels	If TRUE, the y-axis ticks and labels will be shown. Default TRUE.
same_scale	If TRUE, the scale of the y-axis for each sample will be the same. If FALSE, then the scale of the y-axis will be adjusted for each sample. Default TRUE.
annotation	Vector of annotations to be displayed in the top right corner of each sample. Vector length must be equivalent to the number of samples. Default NULL.

Value

Generates a ggplot object

Examples

```
data(musica_sbs96)
plot_sample_counts(musica_sbs96, sample_names =
  sample_names(musica_sbs96)[1])
```

```
plot_sample_reconstruction_error
```

Plot reconstruction error for a sample

Description

Displays the observed distribution of counts for each mutation type, the distribution of reconstructed counts for each mutation type using the inferred mutational signatures, and the difference between the two distributions.

Usage

```
plot_sample_reconstruction_error(result, sample, plotly = FALSE)
```

Arguments

result	A <code>musica_result</code> object generated by a mutational discovery or prediction tool.
sample	Name of the sample within the <code>musica_result</code> object.
plotly	If TRUE, the the plot will be made interactive using <code>plotly</code> . Default FALSE.

Value

Generates a ggplot or plotly object

Examples

```
data(res)
plot_sample_reconstruction_error(res, "TCGA-ER-A197-06A-32D-A197-08")
```

plot_signatures	<i>Plots the mutational signatures</i>
-----------------	--

Description

After mutational signature discovery has been performed, this function can be used to display the distribution of each mutational signature. The `color_variable` and `color_mapping` parameters can be used to change the default color scheme of the bars.

Usage

```
plot_signatures(
  result,
  plotly = FALSE,
  color_variable = NULL,
  color_mapping = NULL,
  text_size = 10,
  show_x_labels = TRUE,
  show_y_labels = TRUE,
  same_scale = TRUE,
  y_max = NULL,
  annotation = NULL,
  percent = TRUE
)
```

Arguments

<code>result</code>	A musica_result object generated by a mutational discovery or prediction tool.
<code>plotly</code>	If TRUE, the the plot will be made interactive using plotly . Default FALSE.
<code>color_variable</code>	Name of the column in the variant annotation data.frame to use for coloring the mutation type bars. The variant annotation data.frame can be found within the count table of the musica object. If NULL, then the default column specified in the count table will be used. Default NULL.
<code>color_mapping</code>	A character vector used to map items in the <code>color_variable</code> to a color. The items in <code>color_mapping</code> correspond to the colors. The names of the items in <code>color_mapping</code> should correspond to the unique items in <code>color_variable</code> . If NULL, then the default <code>color_mapping</code> specified in the count table will be used. Default NULL.
<code>text_size</code>	Size of axis text. Default 10.
<code>show_x_labels</code>	If TRUE, the labels for the mutation types on the x-axis will be shown. Default TRUE.
<code>show_y_labels</code>	If TRUE, the y-axis ticks and labels will be shown. Default TRUE.
<code>same_scale</code>	If TRUE, the scale of the probability for each signature will be the same. If FALSE, then the scale of the y-axis will be adjusted for each signature. Default TRUE.

y_max	Vector of maximum y-axis limits for each signature. One value may also be provided to specify a constant y-axis limit for all signatures. Vector length must be 1 or equivalent to the number of signatures. Default NULL.
annotation	Vector of annotations to be displayed in the top right corner of each signature. Vector length must be equivalent to the number of signatures. Default NULL.
percent	If TRUE, the y-axis will be represented in percent format instead of mutation counts. Default TRUE.

Value

Generates a ggplot or plotly object

Examples

```
data(res)
plot_signatures(res)
```

plot_umap	<i>Plot a UMAP from a musica result</i>
-----------	---

Description

Plots samples on a UMAP scatterplot. Samples can be colored by the levels of mutational signatures or by an annotation variable.

Usage

```
plot_umap(
  result,
  color_by = c("signatures", "annotation", "cluster", "none"),
  proportional = TRUE,
  annotation = NULL,
  point_size = 0.7,
  same_scale = TRUE,
  add_annotation_labels = FALSE,
  annotation_label_size = 3,
  annotation_text_box = TRUE,
  plotly = FALSE,
  clust = NULL,
  legend = TRUE,
  strip_axes = FALSE
)
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
color_by	One of "signatures", "annotation", or "none". If "signatures", then one UMAP scatterplot will be generated for each signature and points will be colored by the level of that signature in each sample. If annotation, a single UMAP will be generated colored by the annotation selected using the parameter annotation. If "none", a single UMAP scatterplot will be generated with no coloring. Default "signature".

proportional	If TRUE, then the exposures will be normalized to between 0 and 1 by dividing by the total number of counts for each sample. Default TRUE.
annotation	Sample annotation used to color the points. One used when color_by = "annotation". Default NULL.
point_size	Scatter plot point size. Default 0.7.
same_scale	If TRUE, then all points will share the same color scale in each signature subplot. If FALSE, then each signature subplot will be colored by a different scale with different maximum values. Only used when color_by = "signature". Setting to FALSE is most useful when the maximum value of various signatures are vastly different from one another. Default TRUE.
add_annotation_labels	If TRUE, labels for each group in the annotation variable will be displayed. Only used if color_by = "annotation". This not recommended if the annotation is a continuous variable. The label is plotting using the centroid of each group within the annotation variable. Default FALSE.
annotation_label_size	Size of annotation labels. Only used if color_by = "annotation" and add_annotation_labels = TRUE. Default 3.
annotation_text_box	Place a white box around the annotation labels to improve readability. Only used if color_by = "annotation" and add_annotation_labels = TRUE. Default TRUE.
plotly	If TRUE, the the plot will be made interactive using plotly . Not used if color_by = "signature" and same_scale = FALSE. Default FALSE.
clust	Add cluster labels as annotation
legend	Plot legend
strip_axes	Remove axes labels for cleaner looking plots

Value

Generates a ggplot or plotly object

See Also

See [create_umap](#) to generate a UMAP in a musica result.

Examples

```
data(res_annot)
create_umap(res_annot, "Tumor_Subtypes")
plot_umap(res_annot, "none")
```

predict_exposure	<i>Prediction of exposures in new samples using pre-existing signatures</i>
------------------	---

Description

Exposures for samples will be predicted using an existing set of signatures stored in a `musica_result` object. Algorithms available for prediction include a modify version of "lda", and "decompTumor2Sig".

Usage

```
predict_exposure(
  musica,
  table_name,
  signature_res,
  algorithm = c("lda", "decompTumor2Sig"),
  signatures_to_use = seq_len(ncol(signatures(signature_res))),
  verbose = FALSE
)
```

Arguments

<code>musica</code>	A <code>musica</code> object.
<code>table_name</code>	Name of table used for posterior prediction. Must match the table type used to generate the prediction signatures
<code>signature_res</code>	Signatures used to predict exposures for the samples <code>musica</code> object. Existing signatures need to be stored in a <code>musica_result</code> object.
<code>algorithm</code>	Algorithm to use for prediction of exposures. One of "lda" or "decompTumor2Sig".
<code>signatures_to_use</code>	Which signatures in the <code>signature_res</code> result object to use. Default is to use all signatures.
<code>verbose</code>	If TRUE, progress will be printing. Only used if <code>algorithm = "lda"</code> . Default FALSE.

Value

Returns a `musica_result` object containing signatures given by the `signature_res` parameter and exposures predicted from these signatures.

Examples

```
data(musica)
data(cosmic_v2_sigs)
g <- select_genome("19")
build_standard_table(musica, g, "SBS96", overwrite = TRUE)
result <- predict_exposure(musica = musica, table_name = "SBS96",
  signature_res = cosmic_v2_sigs, algorithm = "lda")

# Predict using LDA-like algorithm with seed set to 1
set.seed(1)
predict_exposure(musica = musica, table_name = "SBS96",
  signature_res = cosmic_v2_sigs, algorithm = "lda")
```

rc	<i>Reverse complement of a string using biostrings</i>
----	--

Description

Reverse complement of a string using biostrings

Usage

```
rc(dna)
```

Arguments

dna Input DNA string

Value

Returns the reverse compliment of the input DNA string

Examples

```
rc("ATGC")
```

rep_range	<i>Replication Timing Data as GRanges Object</i>
-----------	--

Description

Supplementary data converted from bigWig to bedgraph to GRanges, with low RFD indicating the leading strand and high RFD indicating lagging strand and removing uninformative zero RFD intervals. Timing data is 10kb bins from a colon cancer sample.

Usage

```
data(rep_range)
```

Format

An object of class "GRanges"; see [annotate_replication_strand()].

Source

GEO, <<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE134225>>

References

Sriramachandran, A. M. et al. (2020) Genome-wide Nucleotide-Resolution Mapping of DNA Replication Patterns, Single-Strand Breaks, and Lesions by GLOE-Seq. ([Molecular Cell] (doi:10.1016/j.molcel.2020.03

res	<i>res</i>
-----	------------

Description

A musica result created for testing that includes SBS variants with discovered exposures and signatures

Usage

```
data(res)
```

Format

An object of class `musica_result` See `[discover_signatures()]`.

res_annot	<i>res_annot</i>
-----------	------------------

Description

A musica result created for testing that includes SBS variants with annotations and discovered exposures and signatures

Usage

```
data(res_annot)
```

Format

An object of class `musica_result` See `[discover_signatures()]`.

sample_names	<i>Retrieve sample names from a musica or musica_result object</i>
--------------	--

Description

Sample names were included in the sample column in the variant object passed to `create_musica`. This returns a unique list of samples names in the order they are inside the `musica` object.

Usage

```
sample_names(object)

## S4 method for signature 'musica'
sample_names(object)

## S4 method for signature 'musica_result'
sample_names(object)
```

Arguments

object A [musica](#) object generated by the [create_musica](#) function or a [musica_result](#) object generated by a mutational discovery or prediction tool.

Value

A character vector of sample names

Examples

```
data(res)
sample_names(res)
```

samp_annot	<i>Get or set sample annotations from a musica or musica_result object</i>
------------	--

Description

Sample annotations can be used to store information about each sample such as tumor type or treatment status. These are used in downstream plotting functions such as [plot_exposures](#) or [plot_umap](#) to group or color samples by a particular annotation.

Usage

```
samp_annot(object)

## S4 method for signature 'musica'
samp_annot(object)

## S4 method for signature 'musica_result'
samp_annot(object)

samp_annot(object, name) <- value

## S4 replacement method for signature 'musica,character,vector'
samp_annot(object, name) <- value

## S4 replacement method for signature 'musica_result,character,vector'
samp_annot(object, name) <- value
```

Arguments

object A [musica](#) object generated by the [create_musica](#) function or a [musica_result](#) object generated by a mutational discovery or prediction tool.

name The name of the new annotation to add.

value A vector containing the new sample annotations. Needs to be the same length as the number of samples in the object.

Value

A new object with the sample annotations added to the table in the `sample_annotations` slot.

See Also

See `sample_names` to get a vector of sample names in the `musica` or `musica_result` object.

Examples

```
data(res_annot)
samp_annot(res_annot)

# Add new annotation
samp_annot(res_annot, "New_Annotation") <- rep(c("A", "B"), c(3, 4))
samp_annot(res_annot)
data(musica)
samp_annot(musica, "example") <- rep("ex", 7)
```

<code>select_genome</code>	<i>Helper function to load common human or mouse genomes</i>
----------------------------	--

Description

Helper function to load common human or mouse genomes

Usage

```
select_genome(x)
```

Arguments

`x` Select the hg19 or hg38 human genome or the mm9 or mm10 mouse genome in UCSC format

Value

Returns BSgenome of given version

Examples

```
g <- select_genome(x = "hg38")
```

<code>signatures</code>	<i>Retrieve signatures from a musica_result object</i>
-------------------------	--

Description

The signature matrix contains the probability of mutation motif in each sample. Rows correspond to each motif and columns correspond to each signature.

Usage

```
signatures(result)

## S4 method for signature 'musica_result'
signatures(result)

signatures(result) <- value

## S4 replacement method for signature 'musica_result,matrix'
signatures(result) <- value
```

Arguments

result A [musica_result](#) object generated by a mutational discovery or prediction tool.
value A matrix of motifs counts by samples

Value

A matrix of mutational signatures

Examples

```
data(res)
signatures(res)
data(res)
signatures(res) <- matrix()
```

subset_musica_by_annotation

Creates a new musica object subsetted to only one value of a sample annotation

Description

Creates a new musica object subsetted to only one value of a sample annotation

Usage

```
subset_musica_by_annotation(musica, annot_col, annot_names)
```

Arguments

musica A [musica](#) object.
annot_col Annotation class to use for subsetting
annot_names Annotational value to subset to

Value

Returns a new musica object with sample annotations, count tables, and variants subsetted to only contains samples of the specified annotation type

Examples

```
data(musica_sbs96)
annot <- read.table(system.file("extdata", "sample_annotations.txt",
package = "musicatk"), sep = "\t", header=TRUE)

samp_annot(musica_sbs96, "Tumor_Subtypes") <- annot$Tumor_Subtypes

musica_sbs96 <- subset_musica_by_annotation(musica_sbs96, "Tumor_Subtypes",
"Lung")
```

subset_musica_by_counts

Creates a new musica subsetting to only samples with enough variants

Description

Creates a new musica subsetting to only samples with enough variants

Usage

```
subset_musica_by_counts(musica, table_name, num_counts)
```

Arguments

musica	A musica object.
table_name	Name of table used for subsetting
num_counts	Minimum sum count value to drop samples

Value

Returns a new musica object with sample annotations, count tables, and variants subsetting to only contains samples with the specified minimum number of counts (column sums) in the specified table

Examples

```
data(musica_sbs96)
subset_musica_by_counts(musica_sbs96, "SBS96", 20)
```

`subset_variants_by_samples`*Return sample from musica_variant object*

Description

Return sample from musica_variant object

Usage

```
subset_variants_by_samples(musica, sample_name)
```

Arguments

<code>musica</code>	A <code>musica</code> object.
<code>sample_name</code>	Sample name to subset by

Value

Returns sample data.frame subset to a single sample

Examples

```
data(musica)
subset_variants_by_samples(musica, "TCGA-94-7557-01A-11D-2122-08")
```

`subset_variant_by_type`*Subsets a variant table based on Variant Type*

Description

Subsets a variant table based on Variant Type

Usage

```
subset_variant_by_type(tab, type)
```

Arguments

<code>tab</code>	Input variant table
<code>type</code>	Variant type to return e.g. "SBS", "INS", "DEL", "DBS"

Value

Returns the input variant table subsetted to only contain variants of the specified variant type

Examples

```
data(musica)
annotate_variant_type(musica)
subset_variant_by_type(variants(musica), "SBS")
```

tables	<i>Retrieve the list of count_tables from a musica or musica_result object</i>
--------	--

Description

The count_tables contains standard and/or custom count tables created from variants

Usage

```
tables(object)

## S4 method for signature 'musica'
tables(object)

## S4 method for signature 'musica_result'
tables(object)

tables(musica) <- value

## S4 replacement method for signature 'musica,list'
tables(musica) <- value
```

Arguments

object	A musica object generated by the create_musica function or a musica_result object generated by a mutational discovery or prediction tool.
musica	A musica object generated by the create_musica function or a musica_result object generated by a mutational discovery or prediction tool.
value	A list of count_table objects representing counts of motifs in samples

Value

A list of count_tables

Examples

```
data(res)
tables(res)
data(musica)
tables(musica)
```

table_96	<i>Generates a 96 motif table based on input counts for plotting</i>
----------	--

Description

Generates a 96 motif table based on input counts for plotting

Usage

```
table_96(sample_df)
```

Arguments

sample_df Input counts table

Value

Returns a 96 motif summary table

table_selected	<i>Retrieve table name used for plotting from a musica_result object</i>
----------------	--

Description

The table name

Usage

```
table_selected(result)  
  
## S4 method for signature 'musica_result'  
table_selected(result)
```

Arguments

result A [musica_result](#) object generated by a mutational discovery or prediction tool.

Value

Table name used for plotting

Examples

```
data(res)  
table_selected(res)
```

umap	<i>Retrieve umap list from a musica_result object</i>
------	---

Description

The signature matrix contains the probability of mutation motif in each sample. Rows correspond to each motif and columns correspond to each signature.

Usage

```
umap(result)

## S4 method for signature 'musica_result'
umap(result)

umap(result) <- value

## S4 replacement method for signature 'musica_result,matrix'
umap(result) <- value
```

Arguments

result	A musica_result object generated by a mutational discovery or prediction tool.
value	A list of umap dataframes

Value

A list of umap dataframes

Examples

```
data(res)
umap(res)
data(res)
umap(res) <- matrix()
```

variants	<i>Retrieve variants from a musica or musica_result object</i>
----------	--

Description

The variants `data.table` contains the variants and variant-level annotations

Usage

```

variants(object)

## S4 method for signature 'musica'
variants(object)

## S4 method for signature 'musica_result'
variants(object)

variants(musica) <- value

## S4 replacement method for signature 'musica,data.table'
variants(musica) <- value

```

Arguments

object	A musica object generated by the create_musica function or a musica_result object generated by a mutational discovery or prediction tool.
musica	A musica object generated by the create_musica function
value	A data.table of mutational variants and variant-level annotations

Value

A [data.table](#) of variants

Examples

```

data(res)
variants(res)
data(musica)
variants(musica)

```

%>%

Pipe operator

Description

Pipe operator

Usage

```
lhs %>% rhs
```

Value

NA

Examples

```
c(1,2) %>% barplot()
```

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