

Package ‘musicatk’

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Type Package

Title Mutational Signature Comprehensive Analysis Toolkit

Version 1.8.0

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.

License LGPL-3

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

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

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)
```

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 <code>musica</code> 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", "DEL", "DBS")*

Description

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

Usage

```
annotate_variant_type(musica)
```

Arguments

musica A [musica](#) object.

Value

None

Examples

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

auto_predict_grid *Automatic filtering of signatures for exposure prediction gridded across specific annotation*

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", decompTumor2Sig, and deconstructSigs |
| 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")
```

| | |
|--------------------|---|
| 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 | <i>Perform clustering analysis from a musica result object</i> |
|------------------|--|

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))
)
```

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 |

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))
)
```

Arguments

| | |
|---------------|---|
| result | A <code>musica_result</code> 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 |

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))
)
```


Arguments

| | |
|-------------------|---|
| result | A <code>musica_result</code> object. |
| other_result | A second <code>musica_result</code> 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 |

Value

Returns the comparisons

Examples

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

| | |
|----------------|---|
| cosmic_v2_sigs | <i>COSMIC v2 SBS96 Signatures Result Object</i> |
|----------------|---|

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

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.

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_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

- x A data.table, matrix, or data.frame that contains columns with the variant information.
- genome A [BSgenome](#) object indicating which genome reference the variants and their coordinates were derived from.

| | |
|-----------------------|--|
| check_ref_chromosomes | 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 <code>seqlevelsStyle</code> function will be made. Default TRUE. |
| check_ref_bases | Whether to check if the reference bases in the variant object match the reference bases in the genome object. Default TRUE. |
| chromosome_col | The name of the column that contains the chromosome reference for each variant. Default "chr". |
| start_col | The name of the column that contains the start position for each variant. Default "start". |
| 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 'CACA > -') |
| 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_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)
```

`dbm_musica``dbm_musica`

Description

A musica created for testing that includes DBS variants

Usage

```
data(dbm_musica)
```

Format

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

`discover_signatures``Discover mutational signatures`

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 [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

Retrieve exposures from a musica_result object

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`*Compare exposures of annotated samples*

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

| | |
|----------------------------|--|
| <code>musica_result</code> | A <code>musica_result</code> object |
| <code>annotation</code> | Column in the <code>sample_annotations</code> table of the <code>musica_result</code> object |
| <code>method</code> | Any method in <code>c("wilcox", "kruskal", "glm.nb")</code> used to perform differential analysis on signature exposures |
| <code>group1</code> | character vector used in the Wilcox test. Elements in <code>group1</code> are compared to elements in <code>group2</code> . This is required for annotation with more than 2 levels. |
| <code>group2</code> | character vector used in the Wilcox test. Elements in <code>group2</code> are compared to elements in <code>group1</code> . This is required for annotation with more than 2 levels. |
| <code>...</code> | 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 *Extract variants from multiple objects*

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

| | |
|-----------------|--|
| inputs | 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. |
| id | 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> . |
| rename | 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 <code>##SAMPLE</code> portion of header in the VCF. See extract_variants_from_vcf for more details. Default <code>NULL</code> . |
| filename_as_id | If set to <code>TRUE</code> , 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 <code>TRUE</code> . |
| strip_extension | Only used if <code>filename_as_id</code> is set to <code>TRUE</code> . If set to <code>TRUE</code> , 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 <code>c(".vcf", ".vcf.gz", ".gz")</code> |
| filter | Exclude variants that do not have a <code>PASS</code> in the <code>FILTER</code> 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 <code>"expand"</code> . |
| 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 <code>TRUE</code> . |
| extra_fields | Optionally extract additional fields from all input objects. Default <code>NULL</code> . |
| chromosome_col | The name of the column that contains the chromosome reference for each variant. Only used if the input is a <code>matrix</code> or <code>data.frame</code> . Default <code>"Chromosome"</code> . |
| start_col | The name of the column that contains the start position for each variant. Only used if the input is a <code>matrix</code> or <code>data.frame</code> . Default <code>"Start_Position"</code> . |
| end_col | The name of the column that contains the end position for each variant. Only used if the input is a <code>matrix</code> or <code>data.frame</code> . Default <code>"End_Position"</code> . |

| | |
|------------|---|
| 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 loations 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

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

| | |
|------------------------------|---|
| <code>vcf_file</code> | Path to the vcf file |
| <code>id</code> | ID of the sample to select from VCF. If NULL, then the first sample will be selected. Default NULL. |
| <code>rename</code> | Rename the sample to this value when extracting variants. If NULL, then the sample will be named according to ID. |
| <code>sample_field</code> | 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 <code>id</code> parameter ("TUMOR" in this example), then <code>sample_field</code> can be used to specify the name of the tag ("SampleName" in this example). Default NULL. |
| <code>filename_as_id</code> | If set to TRUE, the file name will be used as the sample name. |
| <code>strip_extension</code> | Only used if <code>filename_as_id</code> 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 <code>c(".vcf", ".vcf.gz", ".gz")</code> |
| <code>filter</code> | Exclude variants that do not have a PASS in the FILTER column of the VCF. Default TRUE. |
| <code>multiallele</code> | 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". |
| <code>extra_fields</code> | Optionally extract additional fields from the INFO section of the VCF. Default NULL. |
| <code>fix_vcf_errors</code> | 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` object 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` object

Examples

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

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

Description

A `musica` object created for testing that includes INDEL variants

Usage

```
data(indel_musica)
```

Format

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

k_select

*Plots for helping decide number of clusters***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 | <i>musica</i> |
|--------|---------------|

Description

A musica created for testing that includes SBS variants

Usage

```
data(musica)
```

Format

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

| | |
|--------------|---|
| musica-class | <i>The primary object that contains variants, count_tables, and samples annotations</i> |
|--------------|---|

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 | <i>Object containing deconvolved/predicted signatures, sample weights, and the musica object the result was generated from</i> |
|---------------------|--|

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 cluster_exposure 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 | <i>Display sample exposures with bar, box, or violin plots</i> |
|----------------|--|

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

| | |
|---------------------------|---|
| <code>result</code> | A <code>musica_result</code> object generated by a mutational discovery or prediction tool. |
| <code>plot_type</code> | One of "bar", "box", or "violin". Default "bar". |
| <code>proportional</code> | 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. |
| <code>group_by</code> | 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 <code>annotation</code> parameter. Default "none". |
| <code>color_by</code> | 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 <code>annotation</code> parameter. Default "signature". |
| <code>annotation</code> | 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 <code>mixedsort</code> 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 <code>plotly</code> . 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)
```

Arguments

| | |
|--------------|--|
| musica | A musica 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 musica object will be used. 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 musica_result object generated by a mutational discovery or prediction tool. |
| sample | Name of the sample within the musica_result object. |
| plotly | If TRUE, the the plot will be made interactive using plotly . 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,
  legend = TRUE,
  plotly = FALSE,
  color_variable = NULL,
  color_mapping = NULL,
  text_size = 10,
  facet_size = 10,
  show_x_labels = TRUE,
  same_scale = TRUE
)
```

Arguments

| | |
|-----------------------------|---|
| <code>result</code> | A <code>musica_result</code> object generated by a mutational discovery or prediction tool. |
| <code>legend</code> | If TRUE, the legend for mutation types will be included in the plot. Default TRUE. |
| <code>plotly</code> | If TRUE, the the plot will be made interactive using <code>plotly</code> . 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 <code>musica</code> 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. |

| | |
|---------------|--|
| text_size | Size of axis text. Default 10. |
| facet_size | Size of facet text. Default 10. |
| show_x_labels | If TRUE, the labels for the mutation types on the x-axis will be shown. Default TRUE. |
| 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

Generates a ggplot or plotly object

Examples

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

plot_umap

Plot a UMAP from a musica result

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 <code>musica_result</code> 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 codecolor_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 codecolor_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 codecolor_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", "decompTumor2Sig", and "deconstructSigs".

Usage

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

Arguments

| | |
|-------------------|---|
| musica | A musica object. |
| g | A BSgenome object indicating which genome reference the variants and their coordinates were derived from. Only used if <code>algorithm = "deconstructSigs"</code> |
| table_name | Name of table used for posterior prediction. Must match the table type used to generate the prediction signatures |
| signature_res | Signatures used to predict exposures for the samples musica object. Existing signatures need to be stored in a musica_result object. |
| algorithm | Algorithm to use for prediction of exposures. One of "lda", "decompTumor2Sig", or "deconstructSigs". |
| signatures_to_use | Which signatures in the signature_res result object to use. Default is to use all signatures. |
| verbose | 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 *Reverse complement of a string using biostrings*

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 *Replication Timing Data as GRanges Object*

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.2020.03.027

| | |
|-----|------------|
| 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 <code>musica</code> object generated by the <code>create_musica</code> function or a <code>musica_result</code> 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)
```

| | |
|---------------|--|
| select_genome | <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")
```

| | |
|------------|--|
| signatures | <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

| | |
|-------------------------|---|
| <code>musica</code> | A <code>musica</code> object. |
| <code>table_name</code> | Name of table used for subsetting |
| <code>num_counts</code> | 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

| | |
|------|--|
| tab | Input variant table |
| type | 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_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)
```


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