

Package ‘MutationalPatterns’

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Type Package

Title Comprehensive genome-wide analysis of mutational processes

Description An extensive toolset for the characterization and visualization of a wide range of mutational patterns in base substitution catalogs.

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binomial_test	<i>Binomial test for enrichment or depletion testing</i>
---------------	--

Description

This function performs lower-tail binomial test for depletion and upper-tail test for enrichment

Usage

```
binomial_test(p, n, x)
```

Arguments

p	Probability of success
n	Number of trials
x	Observed number of successes

Value

A data.frame with direction of effect (enrichment/depletion), P-value and significance asterisks

Examples

```
binomial_test (0.5, 1200, 543)
binomial_test (0.2, 800, 150)
```

cluster_signatures *Signature clustering function*

Description

Hierarchical clustering of signatures based on cosine similarity

Usage

```
cluster_signatures(signatures, method = "complete")
```

Arguments

signatures	Matrix with 96 trinucleotides (rows) and any number of signatures (columns)
method	The agglomeration method to be used for hierarchical clustering. This should be one of "ward.D", "ward.D2", "single", "complete", "average" (= UPGMA), "mcquitty" (= WPGMA), "median" (= WPGMC) or "centroid" (= UPGMC). Default = "complete".

Value

hclust object

See Also

[plot_contribution_heatmap](#)

Examples

```
## You can download mutational signatures from the COSMIC database:
# sp_url = http://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt
# cancer_signatures = read.table(sp_url, sep = "\t", header = T)

## We copied the file into our package for your convenience.
filename <- system.file("extdata/signatures_probabilities.txt",
  package="MutationalPatterns")
cancer_signatures <- read.table(filename, sep = "\t", header = TRUE)
```

```
## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                             package="MutationalPatterns"))

## Match the order to MutationalPatterns standard of mutation matrix
order = match(row.names(mut_mat), cancer_signatures$Somatic.Mutation.Type)
## Reorder cancer signatures dataframe
cancer_signatures = cancer_signatures[order,]
## Use trinucleotide changes names as row.names
## row.names(cancer_signatures) = cancer_signatures$Somatic.Mutation.Type
## Keep only 96 contributions of the signatures in matrix
cancer_signatures = as.matrix(cancer_signatures[,4:33])
## Rename signatures to number only
colnames(cancer_signatures) = as.character(1:30)

## Hierarchically cluster the cancer signatures based on cosine similarity
hclust_cancer_signatures = cluster_signatures(cancer_signatures)

## Plot dendrogram
plot(hclust_cancer_signatures)

## Save the signature names in the order of the clustering
sig_order = colnames(cancer_signatures)[hclust_cancer_signatures$order]
```

cos_sim

Cosine similarity function

Description

Calculate the cosine similarity between two vectors of the same length. The cosine similarity is a value between 0 (distinct) and 1 (identical) and indicates how much two vectors are alike.

Usage

```
cos_sim(x, y)
```

Arguments

x	Vector 1 of length n
y	Vector 2 of length n

Value

Cosine similarity value; a value between 0 and 1

Examples

```
x = c(1.1, 2.1, 0.2, 0.1, 2.9)
y = c(0.9, 1.9, 0.5, 0.4, 3.1)
cos_sim(x, y)
```

cos_sim_matrix	<i>Compute all pairwise cosine similarities between mutational profiles/signatures</i>
----------------	--

Description

Computes all pairwise cosine similarities between the mutational profiles provided in the two mutation count matrices. The cosine similarity is a value between 0 (distinct) and 1 (identical) and indicates how much two vectors are alike.

Usage

```
cos_sim_matrix(mut_matrix1, mut_matrix2)
```

Arguments

mut_matrix1	96 mutation count matrix (dimensions: 96 mutations X n samples)
mut_matrix2	96 mutation count matrix (dimensions: 96 mutations X m samples)

Value

Matrix with pairwise cosine similarities (dimensions: n mutational profiles X m mutational profiles)

See Also

[mut_matrix](#), [fit_to_signatures](#), [plot_cosine_heatmap](#)

Examples

```
## You can download mutational signatures from the COSMIC database:
# sp_url = http://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt
# cancer_signatures = read.table(sp_url, sep = "\t", header = T)

## We copied the file into our package for your convenience.
filename <- system.file("extdata/signatures_probabilities.txt",
  package="MutationalPatterns")
cancer_signatures <- read.table(filename, sep = "\t", header = TRUE)

## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
  package="MutationalPatterns"))

## Match the order to MutationalPatterns standard of mutation matrix
order = match(row.names(mut_mat), cancer_signatures$Somatic.Mutation.Type)
## Reorder cancer signatures dataframe
cancer_signatures = cancer_signatures[order,]
## Use trinucleotide changes names as row.names
## row.names(cancer_signatures) = cancer_signatures$Somatic.Mutation.Type
## Keep only 96 contributions of the signatures in matrix
cancer_signatures = as.matrix(cancer_signatures[,4:33])
## Rename signatures to number only
colnames(cancer_signatures) = as.character(1:30)
```

```
## Calculate the cosine similarity between each COSMIC signature and each 96 mutational profile
cos_sim_matrix(mut_mat, cancer_signatures)
```

```
enrichment_depletion_test
```

Test for enrichment or depletion of mutations in genomic regions

Description

This function aggregates mutations per group (optional) and performs an enrichment depletion test.

Usage

```
enrichment_depletion_test(x, by = c())
```

Arguments

x	data.frame result from <code>genomic_distribution()</code>
by	Optional grouping variable, e.g. tissue type

Value

data.frame with the observed and expected number of mutations per genomic region per group (by) or sample

See Also

[genomic_distribution](#), [plot_enrichment_depletion](#)

Examples

```
## See the 'genomic_distribution()' example for how we obtained the
## following data:
distr <- readRDS(system.file("states/distr_data.rds",
                             package="MutationalPatterns"))

tissue <- c(rep("colon", 3), rep("intestine", 3), rep("liver", 3))

## Perform the enrichment/depletion test by tissue type.
distr_test <- enrichment_depletion_test(distr, by = tissue)

## Or without specifying the 'by' parameter.
distr_test2 <- enrichment_depletion_test(distr)
```

explained_by_signatures

This function has been renamed to 'cos_sim_matrix'.

Description

This function has been renamed to 'cos_sim_matrix'.

Usage

```
explained_by_signatures(mut_matrix, signatures)
```

Arguments

mut_matrix	96 mutation count matrix (dimensions: 96 mutations X n samples)
signatures	96 mutation count matrix (dimensions: 96 mutations X m samples)

Value

Matrix with pairwise cosine similarities

See Also

[cos_sim_matrix](#) [mut_matrix](#), [fit_to_signatures](#), [plot_cosine_heatmap](#)

Examples

```
## You can download mutational signatures from the COSMIC database:
# sp_url = http://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt
# cancer_signatures = read.table(sp_url, sep = "\t", header = T)

## We copied the file into our package for your convenience.
filename <- system.file("extdata/signatures_probabilities.txt",
                        package="MutationalPatterns")
cancer_signatures <- read.table(filename, sep = "\t", header = TRUE)

## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                              package="MutationalPatterns"))

## Match the order to MutationalPatterns standard of mutation matrix
order = match(row.names(mut_mat), cancer_signatures$Somatic.Mutation.Type)
## Reorder cancer signatures dataframe
cancer_signatures = cancer_signatures[order,]
## Use trinucleotide changes names as row.names
## row.names(cancer_signatures) = cancer_signatures$Somatic.Mutation.Type
## Keep only 96 contributions of the signatures in matrix
cancer_signatures = as.matrix(cancer_signatures[,4:33])
## Rename signatures to number only
colnames(cancer_signatures) = as.character(1:30)

## Calculate the cosine similarity between each COSMIC signature and each 96 mutational profile
cos_sim_matrix(mut_mat, cancer_signatures)
```

extract_signatures	<i>Extract mutational signatures from 96 mutation matrix using NMF</i>
--------------------	--

Description

Decomposes trinucleotide count matrix into signatures and contribution of those signatures to the spectra of the samples/vcf files.

Usage

```
extract_signatures(mut_matrix, rank, nrun = 200)
```

Arguments

mut_matrix	96 mutation count matrix
rank	Number of signatures to extract
nrun	Number of iterations, default = 200

Value

Named list of mutation matrix, signatures and signature contribution

See Also

[mut_matrix](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                             package="MutationalPatterns"))

## This function is computational intensive.
# nmf_res <- extract_signatures(mut_mat, rank = 2)
```

fit_to_signatures	<i>Find optimal nonnegative linear combination of mutation signatures to reconstruct the mutation matrix.</i>
-------------------	---

Description

Find the linear combination of mutation signatures that most closely reconstructs the mutation matrix by solving the nonnegative least-squares constraints problem.

Usage

```
fit_to_signatures(mut_matrix, signatures)
```


Arguments

mut_matrix 96 mutation count matrix (dimensions: 96 mutations X n samples)
 signatures Signature matrix (dimensions: 96 mutations X n signatures)

Value

Named list with signature contributions and reconstructed mutation matrix

See Also

[mut_matrix](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                             package="MutationalPatterns"))

## You can download the signatures from the COSMIC website:
# http://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt

## We copied the file into our package for your convenience.
filename <- system.file("extdata/signatures_probabilities.txt",
                       package="MutationalPatterns")
cancer_signatures <- read.table(filename, sep = "\t", header = TRUE)

## Match the order to MutationalPatterns standard of mutation matrix
order = match(row.names(mut_mat), cancer_signatures$Somatic.Mutation.Type)
## Reorder cancer signatures dataframe
cancer_signatures = cancer_signatures[order,]
## Use trinucleotide changes names as row.names
## row.names(cancer_signatures) = cancer_signatures$Somatic.Mutation.Type
## Keep only 96 contributions of the signatures in matrix
cancer_signatures = as.matrix(cancer_signatures[,4:33])
## Rename signatures to number only
colnames(cancer_signatures) = as.character(1:30)

## Perform the fitting
fit_res <- fit_to_signatures(mut_mat, cancer_signatures)
```

genomic_distribution *Find overlaps between mutations and a genomic region.*

Description

Function finds the number of mutations that reside in genomic region and takes surveyed area of genome into account.

Usage

```
genomic_distribution(vcf_list, surveyed_list, region_list)
```



```

## Download the promoter regions and convert them to a GRanges object.
# promoter = getBM(attributes = c('chromosome_name', 'chromosome_start',
#                               'chromosome_end', 'feature_type_name'),
#                 filters = "regulatory_feature_type_name",
#                 values = "Promoter",
#                 mart = regulatory)
# promoter_g = reduce(GRanges(promoter$chromosome_name,
#                             IRanges(promoter$chromosome_start,
#                                     promoter$chromosome_end)))

promoter_g <- readRDS(system.file("states/promoter_g_data.rds",
                                package="MutationalPatterns"))

# open = getBM(attributes = c('chromosome_name', 'chromosome_start',
#                             'chromosome_end', 'feature_type_name'),
#             filters = "regulatory_feature_type_name",
#             values = "Open chromatin",
#             mart = regulatory)
# open_g = reduce(GRanges(open$chromosome_name,
#                         IRanges(open$chromosome_start,
#                                 open$chromosome_end)))

open_g <- readRDS(system.file("states/open_g_data.rds",
                             package="MutationalPatterns"))

# flanking = getBM(attributes = c('chromosome_name',
#                                 'chromosome_start',
#                                 'chromosome_end',
#                                 'feature_type_name'),
#                 filters = "regulatory_feature_type_name",
#                 values = "Promoter Flanking Region",
#                 mart = regulatory)
# flanking_g = reduce(GRanges(
#                 flanking$chromosome_name,
#                 IRanges(flanking$chromosome_start,
#                         flanking$chromosome_end)))

flanking_g <- readRDS(system.file("states/promoter_flanking_g_data.rds",
                                 package="MutationalPatterns"))

# TF_binding = getBM(attributes = c('chromosome_name', 'chromosome_start',
#                                  'chromosome_end', 'feature_type_name'),
#                   filters = "regulatory_feature_type_name",
#                   values = "TF binding site",
#                   mart = regulatory)
# TF_binding_g = reduce(GRanges(TF_binding$chromosome_name,
#                               IRanges(TF_binding$chromosome_start,
#                                       TF_binding$chromosome_end)))

TF_binding_g <- readRDS(system.file("states/TF_binding_g_data.rds",
                                   package="MutationalPatterns"))

regions <- GRangesList(promoter_g, flanking_g, CTCF_g, open_g, TF_binding_g)

names(regions) <- c("Promoter", "Promoter flanking", "CTCF",
                  "Open chromatin", "TF binding")

```

```
# Use a naming standard consistently.
seqlevelsStyle(regions) <- "UCSC"

## Get the filename with surveyed/callable regions
surveyed_file <- system.file("extdata/callableloci-sample.bed",
                             package="MutationalPatterns")

## Import the file using rtracklayer and use the UCSC naming standard
library(rtracklayer)
surveyed <- import(surveyed_file)
seqlevelsStyle(surveyed) <- "UCSC"

## For this example we use the same surveyed file for each sample.
surveyed_list <- rep(list(surveyed), 9)

## Calculate the number of observed and expected number of mutations in
## each genomic regions for each sample.
distr <- genomic_distribution(vcfs, surveyed_list, regions)
```

MutationalPatterns *MutationalPatterns: an integrative R package for studying patterns in base substitution catalogues*

Description

This package provides an extensive toolset for the characterization and visualization of a wide range of mutational patterns from base substitution catalogues. These patterns include: mutational signatures, transcriptional strand bias, genomic distribution and association with genomic features.

Details

The package provides functionalities for both extracting mutational signatures de novo and inferring the contribution of previously identified mutational signatures. Furthermore, MutationalPatterns allows for easy exploration and visualization of other types of patterns such as transcriptional strand asymmetry, genomic distribution and associations with (publically available) annotations such as chromatin organization. In addition to identification of active mutation-inducing processes, this approach also allows for determining the involvement of specific DNA repair pathways. For example, presence of a transcriptional strand bias in genic regions may indicate activity of transcription coupled repair.

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See Also

<https://github.com/CuppenResearch/MutationalPatterns>

mutations_from_vcf *Retrieve base substitutions from vcf*

Description

A function to extract base substitutions of each position in vcf

Usage

```
mutations_from_vcf(vcf)
```

Arguments

vcf A CollapsedVCF object

Value

Character vector with base substitutions

See Also

[read_vcfs_as_granges](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                             package="MutationalPatterns"))

muts = mutations_from_vcf(vcfs[[1]])
```

mutation_context *This function has been removed. Use 'mut_context' instead.*

Description

This function has been removed. Use 'mut_context' instead.

Usage

```
mutation_context(vcf, ref_genome)
```

Arguments

vcf A GRanges object
ref_genome The reference genome

Value

Character vector with the context of the base substitutions

See Also

[mut_context](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the  
## following data:  
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",  
                            package="MutationalPatterns"))  
  
## Load the corresponding reference genome.  
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"  
library(ref_genome, character.only = TRUE)  
  
mut_context <- mut_context(vcfs[[1]], ref_genome)
```

mutation_types *This function has been renamed. Use 'mut_type' instead.*

Description

This function has been renamed. Use 'mut_type' instead.

Usage

```
mutation_types(vcf)
```

Arguments

vcf A GRanges object.

Value

Character vector with base substitution types

See Also

[read_vcfs_as_granges](#) [mut_type](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

mut_type(vcfs[[1]])
```

mut_context

Retrieve context of base substitutions

Description

A function to extract the bases 3' upstream and 5' downstream of the base substitutions from the reference genome

Usage

```
mut_context(vcf, ref_genome)
```

Arguments

vcf A Granges object
ref_genome Reference genome

Value

Character vector with the context of the base substitutions

See Also

[read_vcfs_as_granges](#),

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## Load the corresponding reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

mut_context <- mut_context(vcfs[[1]], ref_genome)
```

mut_matrix

Make mutation count matrix of 96 trinucleotides

Description

Make 96 trinucleotide mutation count matrix

Usage

```
mut_matrix(vcf_list, ref_genome)
```

Arguments

vcf_list List of collapsed vcf objects
ref_genome BSGenome reference genome object

Value

96 mutation count matrix

See Also

[read_vcfs_as_granges](#),

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## Load the corresponding reference genome.
ref_genome = "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

## Construct a mutation matrix from the loaded VCFs in comparison to the
## ref_genome.
mut_mat <- mut_matrix(vcf_list = vcfs, ref_genome = ref_genome)
```



```

mut_mat_s = mut_matrix_stranded(vcfs, ref_genome, genes_hg19,
                               mode = "transcription")

## Replication strand analysis:
## Read example bed file with replication direction annotation
repli_file = system.file("extdata/ReplicationDirectionRegions.bed",
                         package = "MutationalPatterns")
repli_strand = read.table(repli_file, header = TRUE)
repli_strand_granges = GRanges(seqnames = repli_strand$Chr,
                              ranges = IRanges(start = repli_strand$Start + 1,
                                                end = repli_strand$Stop),
                              strand_info = repli_strand$Class)

## UCSC seqlevelsstyle
seqlevelsStyle(repli_strand_granges) = "UCSC"
# The levels determine the order in which the features
# will be counted and plotted in the downstream analyses
# You can specify your preferred order of the levels:
repli_strand_granges$strand_info = factor(repli_strand_granges$strand_info, levels = c("left", "right"))

mut_mat_s_rep = mut_matrix_stranded(vcfs, ref_genome, repli_strand_granges,
                                    mode = "replication")

```

mut_strand

Find strand of mutations

Description

Find strand of mutations

Usage

```
mut_strand(vcf, ranges, mode = "transcription")
```

Arguments

vcf	GRanges containing the VCF object
ranges	GRanges object with the genomic ranges of: 1. (transcription mode) the gene bodies with strand (+/-) information, or 2. (replication mode) the replication strand with 'strand_info' metadata
mode	"transcription" or "replication", default = "transcription"

Details

For transcription mode: Definitions of gene bodies with strand (+/-) information should be defined in a GRanges object.

For the base substitutions that are within gene bodies, it is determined whether the "C" or "T" base is on the same strand as the gene definition. (Since by convention we regard base substitutions as C>X or T>X.)

Base substitutions on the same strand as the gene definitions are considered "untranscribed", and on the opposite strand of gene bodies as "transcribed", since the gene definitions report the coding or sense strand, which is untranscribed.

No strand information "-" is returned for base substitutions outside gene bodies, or base substitutions that overlap with more than one gene body on the same strand.

For replication mode: Replication directions of genomic ranges should be defined in GRanges object. The GRanges object should have a "strand_info" metadata column, which contains only two different annotations, e.g. "left" and "right", or "leading" and "lagging". The genomic ranges cannot overlap, to allow only one annotation per location.

For each base substitution it is determined on which strand it is located. No strand information "-" is returned for base substitutions in unannotated genomic regions.

With the package we provide an example dataset, see example code.

Value

Character vector with transcriptional strand information with length of vcf: "-" for positions outside gene bodies, "U" for untranscribed/sense/coding strand, "T" for transcribed/anti-sense/non-coding strand.

See Also

[read_vcfs_as_granges](#),

Examples

```
## For this example we need our variants from the VCF samples, and
## a known genes dataset. See the 'read_vcfs_as_granges()' example
## for how to load the VCF samples.
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## For transcription strand:
## You can obtain the known genes from the UCSC hg19 dataset using
## Bioconductor:
# if (!requireNamespace("BiocManager", quietly=TRUE))
#   install.packages("BiocManager")
# BiocManager::install("TxDb.Hsapiens.UCSC.hg19.knownGene")
# library("TxDb.Hsapiens.UCSC.hg19.knownGene")

## For this example, we preloaded the data for you:
genes_hg19 <- readRDS(system.file("states/genes_hg19.rds",
                                  package="MutationalPatterns"))

mut_strand(vcfs[[1]], genes_hg19, mode = "transcription")

## For replication strand:
## Read example bed file with replication direction annotation
## Read replistrand data
repli_file = system.file("extdata/ReplicationDirectionRegions.bed",
                        package = "MutationalPatterns")
repli_strand = read.table(repli_file, header = TRUE)
repli_strand_granges = GRanges(seqnames = repli_strand$Chr,
                              ranges = IRanges(start = repli_strand$Start + 1,
                                                end = repli_strand$Stop),
                              strand_info = repli_strand$Class)

## UCSC seqlevelsstyle
seqlevelsStyle(repli_strand_granges) = "UCSC"
```

```
mut_strand(vcfs[[1]], repli_strand_granges, mode = "transcription")
```

mut_type	<i>Retrieve base substitution types from a VCF object</i>
----------	---

Description

A function to extract the base substitutions from a vcf and translate to the 6 common base substitution types.

Usage

```
mut_type(vcf)
```

Arguments

vcf A CollapsedVCF object

Value

Character vector with base substitution types

See Also

[read_vcfs_as_granges](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

mut_type(vcfs[[1]])
```

mut_type_occurrences	<i>Count the occurrences of each base substitution type</i>
----------------------	---

Description

Count the occurrences of each base substitution type

Usage

```
mut_type_occurrences(vcf_list, ref_genome)
```

Arguments

vcf_list A GRangesList
ref_genome Reference genome

Value

data.frame with counts of each base substitution type for each sample in `vcf_list`

See Also

[read_vcfs_as_granges](#),

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## Load a reference genome.
ref_genome = "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

## Get the type occurrences for all VCF objects.
type_occurrences = mut_type_occurrences(vcfs, ref_genome)
```

plot_192_profile *Plot 192 trinucleotide profile*

Description

Plot relative contribution of 192 trinucleotides

Usage

```
plot_192_profile(mut_matrix, colors, ymax = 0.2, condensed = FALSE)
```

Arguments

<code>mut_matrix</code>	192 trinucleotide profile matrix
<code>colors</code>	6 value color vector
<code>ymax</code>	Y axis maximum value, default = 0.2
<code>condensed</code>	More condensed plotting format. Default = F.

Value

192 trinucleotide profile plot

See Also

[mut_matrix_stranded](#), [extract_signatures](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## mutation matrix with transcriptional strand information:
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Extract the signatures.
## This is a computationally intensive task, so we load a precomputed
## version instead.
# nmf_res_strand <- extract_signatures(mut_mat_s, rank = 2)
nmf_res_strand <- readRDS(system.file("states/nmf_res_strand_data.rds",
                                      package="MutationalPatterns"))

## Optionally, provide signature names
colnames(nmf_res_strand$signatures) <- c("Signature A", "Signature B")

## Generate the plot
plot_192_profile(nmf_res_strand$signatures)
```

plot_96_profile

Plot 96 trinucleotide profile

Description

Plot relative contribution of 96 trinucleotides

Usage

```
plot_96_profile(mut_matrix, colors, ymax = 0.2, condensed = FALSE)
```

Arguments

mut_matrix	96 trinucleotide profile matrix
colors	6 value color vector
ymax	Y axis maximum value, default = 0.2
condensed	More condensed plotting format. Default = F.

Value

96 trinucleotide profile plot

See Also

[mut_matrix](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## mutation matrix with transcriptional strand information:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                             package="MutationalPatterns"))

## Plot the 96-profile of three samples
plot_96_profile(mut_mat[,c(1,4,7)])
```

plot_compare_profiles *Compare two 96 mutation profiles*

Description

Plots two 96 mutation profiles and their difference, reports the residual sum of squares (RSS).

Usage

```
plot_compare_profiles(profile1, profile2, profile_names = c("profile 1",
  "profile 2"), profile_ymax = 0.2, diff_yylim = c(-0.02, 0.02), colors,
  condensed = FALSE)
```

Arguments

profile1	First 96 mutation profile
profile2	Second 96 mutation profile
profile_names	Character vector with names of the mutations profiles used for plotting, default = c("profile 1", "profile 2")
profile_ymax	Maximum value of y-axis (relative contribution) for profile plotting, default = 0.2
diff_yylim	Y-axis limits for profile difference plot, default = c(-0.02, 0.02)
colors	6 value color vector
condensed	More condensed plotting format. Default = F.

Value

96 spectrum plot of profile 1, profile 2 and their difference

See Also

[mut_matrix](#), [extract_signatures](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the following
## mutation matrix.
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                              package="MutationalPatterns"))

## Extracting signatures can be computationally intensive, so
## we use pre-computed data generated with the following command:
# nmf_res <- extract_signatures(mut_mat, rank = 2)

nmf_res <- readRDS(system.file("states/nmf_res_data.rds",
                              package="MutationalPatterns"))

## Compare the reconstructed 96-profile of sample 1 with original profile
plot_compare_profiles(mut_mat[,1],
                     nmf_res$reconstructed[,1],
                     profile_names = c("Original", "Reconstructed"))
```

plot_contribution *Plot signature contribution barplot*

Description

Plot contribution of signatures

Usage

```
plot_contribution(contribution, signatures, index = c(), coord_flip = FALSE,
                 mode = "relative", palette = c())
```

Arguments

contribution	Signature contribution matrix
signatures	Signature matrix
index	optional sample subset parameter
coord_flip	Flip X and Y coordinates, default = FALSE
mode	"relative" or "absolute"; to plot the relative contribution or absolute number of mutations, default = "relative"
palette	A color palette like c("#FF0000", "#00FF00", "9999CC") that will be used as colors in the plot. By default, ggplot2's colors are used to generate a palette.

Value

Stacked barplot with contribution of each signature for each sample

See Also

[extract_signatures](#), [mut_matrix](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the following
## mutation matrix.
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                              package="MutationalPatterns"))

## Extracting signatures can be computationally intensive, so
## we use pre-computed data generated with the following command:
# nmf_res <- extract_signatures(mut_mat, rank = 2)

nmf_res <- readRDS(system.file("states/nmf_res_data.rds",
                              package="MutationalPatterns"))

## Optionally set column and row names.
colnames(nmf_res$signatures) = c("Signature A", "Signature B")
rownames(nmf_res$contribution) = c("Signature A", "Signature B")

## The following are examples of contribution plots.
plot_contribution(nmf_res$contribution,
                 nmf_res$signature,
                 mode = "relative")

plot_contribution(nmf_res$contribution,
                 nmf_res$signature,
                 mode = "absolute")

plot_contribution(nmf_res$contribution,
                 nmf_res$signature,
                 mode = "absolute",
                 index = c(1,2))

plot_contribution(nmf_res$contribution,
                 nmf_res$signature,
                 mode = "absolute",
                 coord_flip = TRUE)
```

plot_contribution_heatmap

Plot signature contribution heatmap

Description

Plot relative contribution of signatures in a heatmap

Usage

```
plot_contribution_heatmap(contribution, sig_order, cluster_samples = TRUE,
                          method = "complete", plot_values = FALSE)
```

Arguments

contribution Signature contribution matrix

<code>sig_order</code>	Character vector with the desired order of the signature names for plotting. Optional.
<code>cluster_samples</code>	Hierarchically cluster samples based on euclidian distance. Default = T.
<code>method</code>	The agglomeration method to be used for hierarchical clustering. This should be one of "ward.D", "ward.D2", "single", "complete", "average" (= UPGMA), "mcquitty" (= WPGMA), "median" (= WPGMC) or "centroid" (= UPGMC). Default = "complete".
<code>plot_values</code>	Plot relative contribution values in heatmap. Default = F.

Value

Heatmap with relative contribution of each signature for each sample

See Also

[extract_signatures](#), [mut_matrix](#), [plot_contribution](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the following
## mutation matrix.
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
                              package="MutationalPatterns"))

## Extracting signatures can be computationally intensive, so
## we use pre-computed data generated with the following command:

# nmf_res <- extract_signatures(mut_mat, rank = 2)

nmf_res <- readRDS(system.file("states/nmf_res_data.rds",
                              package="MutationalPatterns"))

## Set signature names as row names in the contribution matrix
rownames(nmf_res$contribution) = c("Signature A", "Signature B")

## Define signature order for plotting
sig_order = c("Signature B", "Signature A")

## Contribution heatmap with signatures in defined order
plot_contribution_heatmap(nmf_res$contribution,
                          sig_order = c("Signature B", "Signature A"))

## Contribution heatmap without sample clustering
plot_contribution_heatmap(nmf_res$contribution,
                          sig_order = c("Signature B", "Signature A"),
                          cluster_samples = FALSE, method = "complete")
```

plot_cosine_heatmap *Plot cosine similarity heatmap*

Description

Plot pairwise cosine similarities in a heatmap.

Usage

```
plot_cosine_heatmap(cos_sim_matrix, col_order, cluster_rows = TRUE,
  method = "complete", plot_values = FALSE)
```

Arguments

`cos_sim_matrix` Matrix with pairwise cosine similarities. Result from `cos_sim_matrix`

`col_order` Character vector with the desired order of the columns names for plotting. Optional.

`cluster_rows` Hierarchically cluster rows based on euclidian distance. Default = TRUE.

`method` The agglomeration method to be used for hierarchical clustering. This should be one of "ward.D", "ward.D2", "single", "complete", "average" (= UPGMA), "mcquitty" (= WPGMA), "median" (= WPGMC) or "centroid" (= UPGMC). Default = "complete".

`plot_values` Plot cosine similarity values in heatmap. Default = FALSE.

Value

Heatmap with cosine similarities

See Also

[mut_matrix](#), [cos_sim_matrix](#), [cluster_signatures](#)

Examples

```
## See the 'mut_matrix()' example for how we obtained the mutation matrix:
mut_mat <- readRDS(system.file("states/mut_mat_data.rds",
  package="MutationalPatterns"))

## You can download the signatures from the COSMIC:
# http://cancer.sanger.ac.uk/cancergenome/assets/signatures_probabilities.txt

## We copied the file into our package for your convenience.
filename <- system.file("extdata/signatures_probabilities.txt",
  package="MutationalPatterns")
cancer_signatures <- read.table(filename, sep = "\t", header = TRUE)

## Match the order to MutationalPatterns standard of mutation matrix
order = match(row.names(mut_mat), cancer_signatures$Somatic.Mutation.Type)
## Reorder cancer signatures dataframe
cancer_signatures = cancer_signatures[order,]
## Use trinucleotide changes names as row.names
```

```

## row.names(cancer_signatures) = cancer_signatures$Somatic.Mutation.Type
## Keep only 96 contributions of the signatures in matrix
cancer_signatures = as.matrix(cancer_signatures[,4:33])
## Rename signatures to number only
colnames(cancer_signatures) = as.character(1:30)

## Calculate the cosine similarity between each signature and each 96 mutational profile
cos_matrix = cos_sim_matrix(mut_mat, cancer_signatures)

## Cluster signatures based on cosine similarity
sig_hclust = cluster_signatures(cancer_signatures)
col_order = colnames(cancer_signatures)[sig_hclust$order]

## Plot the cosine similarity between each signature and each sample with hierarchical
## sample clustering and signatures order based on similarity

plot_cosine_heatmap(cos_matrix, col_order, cluster_rows = TRUE, method = "complete")

```

```
plot_enrichment_depletion
```

Plot enrichment/depletion of mutations in genomic regions

Description

Plot enrichment/depletion of mutations in genomic regions

Usage

```
plot_enrichment_depletion(df)
```

Arguments

df Dataframe result from enrichment_depletion_test()

Value

Plot with two parts. 1: Barplot with no. mutations expected and observed per region. 2: Effect size of enrichment/depletion (log2ratio) with results significance test.

See Also

[enrichment_depletion_test](#), [genomic_distribution](#)

Examples

```

## See the 'genomic_distribution()' example for how we obtained the
## following data:
distr <- readRDS(system.file("states/distr_data.rds",
                             package="MutationalPatterns"))

tissue = c( "colon", "colon", "colon",
            "intestine", "intestine", "intestine",
            "liver", "liver", "liver" )

```

```
## Perform the enrichment/depletion test.
distr_test = enrichment_depletion_test(distr, by = tissue)
distr_test2 = enrichment_depletion_test(distr)

## Plot the enrichment/depletion
plot_enrichment_depletion(distr_test)
plot_enrichment_depletion(distr_test2)
```

plot_rainfall *Plot genomic rainfall*

Description

Rainfall plot visualizes the types of mutations and intermutation distance

Usage

```
plot_rainfall(vcf, chromosomes, title = "", colors, cex = 2.5,
              cex_text = 3, ylim = 1e+08)
```

Arguments

vcf	CollapsedVCF object
chromosomes	Vector of chromosome/contig names of the reference genome to be plotted
title	Optional plot title
colors	Vector of 6 colors used for plotting
cex	Point size
cex_text	Text size
ylim	Maximum y value (genomic distance)

Details

Rainfall plots can be used to visualize the distribution of mutations along the genome or a subset of chromosomes. The distance of a mutation with the mutation prior to it (the intermutation distance) is plotted on the y-axis on a log scale.

The colour of the points indicates the base substitution type. Clusters of mutations with lower intermutation distance represent mutation hotspots.

Value

Rainfall plot

See Also

[read_vcfs_as_granges](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

# Specify chromosomes of interest.
chromosomes = names(genome(vcfs[[1]])[1:22])

## Do a rainfall plot for all chromosomes:
plot_rainfall(vcfs[[1]],
              title = names(vcfs[1]),
              chromosomes = chromosomes,
              cex = 1)

## Or for a single chromosome (chromosome 1):
plot_rainfall(vcfs[[1]],
              title = names(vcfs[1]),
              chromosomes = chromosomes[1],
              cex = 2)
```

plot_signature_strand_bias
Plot signature strand bias

Description

Plot strand bias per mutation type for each signature.

Usage

```
plot_signature_strand_bias(signatures_strand_bias)
```

Arguments

```
signatures_strand_bias  
Signature matrix with 192 features
```

Value

Barplot

See Also

```
link{extract_signatures}, link{mut_matrix()}
```

Examples

```
## See the 'mut_matrix()' example for how we obtained the following
## mutation matrix.
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Extracting signatures can be computationally intensive, so
## we use pre-computed data generated with the following command:
# nmf_res_strand <- extract_signatures(mut_mat_s, rank = 2)

nmf_res_strand <- readRDS(system.file("states/nmf_res_strand_data.rds",
                                     package="MutationalPatterns"))

## Provide column names for the plot.
colnames(nmf_res_strand$signatures) = c("Signature A", "Signature B")

plot_signature_strand_bias(nmf_res_strand$signatures)
```

plot_spectrum	<i>Plot point mutation spectrum</i>
---------------	-------------------------------------

Description

Plot point mutation spectrum

Usage

```
plot_spectrum(type_occurrences, CT = FALSE, by, colors, legend = TRUE)
```

Arguments

type_occurrences	Type occurrences matrix
CT	Distinction between C>T at CpG and C>T at other sites, default = FALSE
by	Optional grouping variable
colors	Optional color vector with 7 values
legend	Plot legend, default = TRUE

Value

Spectrum plot

See Also

[read_vcfs_as_granges](#), [mut_type_occurrences](#)

Examples

```

## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## Load a reference genome.
ref_genome = "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

## Get the type occurrences for all VCF objects.
type_occurrences = mut_type_occurrences(vcfs, ref_genome)

## Plot the point mutation spectrum over all samples
plot_spectrum(type_occurrences)

## Or with distinction of C>T at CpG sites
plot_spectrum(type_occurrences, CT = TRUE)

## Or without legend
plot_spectrum(type_occurrences, CT = TRUE, legend = FALSE)

## Or plot spectrum per tissue
tissue <- c("colon", "colon", "colon",
           "intestine", "intestine", "intestine",
           "liver", "liver", "liver")
plot_spectrum(type_occurrences, by = tissue, CT = TRUE)

## You can also set custom colors.
my_colors = c("pink", "orange", "blue", "lightblue",
             "green", "red", "purple")

## And use them in a plot.
plot_spectrum(type_occurrences,
             CT = TRUE,
             legend = TRUE,
             colors = my_colors)

```

plot_strand

Plot strand per base substitution type

Description

For each base substitution type and transcriptional strand the total number of mutations and the relative contribution within a group is returned.

Usage

```
plot_strand(strand_bias_df, mode = "relative", colors)
```


Arguments

strand_bias_df data.frame, result from strand_bias function
 mode Either "absolute" for absolute number of mutations, or "relative" for relative contribution, default = "relative"
 colors Optional color vector for plotting with 6 values

Value

Barplot

See Also

[mut_matrix_stranded](#), [strand_occurrences](#), [plot_strand_bias](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## following mutation matrix.
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Load a reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

tissue <- c("colon", "colon", "colon",
            "intestine", "intestine", "intestine",
            "liver", "liver", "liver")

strand_counts = strand_occurrences(mut_mat_s, by=tissue)

#' ## Plot the strand in relative mode.
strand_plot = plot_strand(strand_counts)

#' ## Or absolute mode.
strand_plot = plot_strand(strand_counts, mode = "absolute")
```

plot_strand_bias *Plot strand bias per base substitution type per group*

Description

Plot strand bias per base substitution type per group

Usage

```
plot_strand_bias(strand_bias, colors)
```

Arguments

strand_bias data.frame, result from strand_bias function
 colors Optional color vector with 6 values for plotting

Value

Barplot

See Also

[mut_matrix_stranded](#), [strand_occurrences](#), [strand_bias_test](#) [plot_strand](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## following mutation matrix.
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Load a reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

tissue <- c("colon", "colon", "colon",
            "intestine", "intestine", "intestine",
            "liver", "liver", "liver")

## Perform the strand bias test.
strand_counts = strand_occurrences(mut_mat_s, by=tissue)
strand_bias = strand_bias_test(strand_counts)

## Plot the strand bias.
plot_strand_bias(strand_bias)
```

read_vcfs_as_granges *Read VCF files into a GRangesList*

Description

This function reads Variant Call Format (VCF) files into a GRanges object and combines them in a GRangesList. In addition to loading the files, this function applies the same seqlevel style to the GRanges objects as the reference genome passed in the 'genome' parameter.

Usage

```
read_vcfs_as_granges(vcf_files, sample_names, genome, group = "auto+sex",
                     check_alleles = TRUE)
```

Arguments

vcf_files	Character vector of VCF file names
sample_names	Character vector of sample names
genome	A string matching the name of a BSgenome library corresponding to the reference genome of your VCFs

- group** Selector for a seqlevel group. All seqlevels outside of this group will be removed. Possible values: * 'all' for all chromosomes; * 'auto' for autosomal chromosomes; * 'sex' for sex chromosomes; * 'auto+sex' for autosomal + sex chromosomes (default); * 'circular' for circular chromosomes; * 'none' for no filtering, which results in keeping all seqlevels from the VCF file.
- check_alleles** logical. If TRUE (default) positions with insertions, deletions and/or multiple alternative alleles are excluded from the vcf object, since these positions cannot be analysed with this package. This setting can be set to FALSE to speed up processing time only if the input vcf does not contain any of such positions, as these will cause obscure errors.

Value

A GRangesList containing the GRanges obtained from 'vcf_files'

Examples

```
# The example data set consists of three colon samples, three intestine
# samples and three liver samples. So, to map each file to its appropriate
# sample name, we create a vector containing the sample names:
sample_names <- c( "colon1", "colon2", "colon3",
                  "intestine1", "intestine2", "intestine3",
                  "liver1", "liver2", "liver3" )

# We assemble a list of files we want to load. These files match the
# sample names defined above.
vcf_files <- list.files(system.file("extdata",
                                   package="MutationalPatterns"),
                       pattern = ".vcf", full.names = TRUE)

# Get a reference genome BSgenome object.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library("BSgenome")
library(ref_genome, character.only = TRUE)

# This function loads the files as GRanges objects
vcfs <- read_vcfs_as_granges(vcf_files, sample_names, ref_genome)
```

strand_bias_test *Significance test for strand asymmetry*

Description

This function performs a Poisson test for the ratio between mutations on each strand

Usage

```
strand_bias_test(strand_occurrences)
```

Arguments

strand_occurrences
Dataframe with mutation count per strand, result from strand_occurrences()

Value

Dataframe with poisson test P value for the ratio between the two strands per group per base substitution type.

See Also

[mut_matrix_stranded](#), [strand_occurrences](#), [plot_strand_bias](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## following mutation matrix.
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Load a reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

tissue <- c("colon", "colon", "colon",
            "intestine", "intestine", "intestine",
            "liver", "liver", "liver")

## Perform the strand bias test.
strand_counts = strand_occurrences(mut_mat_s, by=tissue)
strand_bias = strand_bias_test(strand_counts)
```

strand_from_vcf

This function has been renamed. Use 'mut_strand' instead.

Description

This function has been renamed. Use 'mut_strand' instead.

Usage

```
strand_from_vcf(vcf, genes)
```

Arguments

vcf	A GRanges object
genes	The genes

Value

Character vector with transcriptional strand information

See Also

[mut_strand](#)

strand_occurrences	<i>Count occurrences per base substitution type and strand</i>
--------------------	--

Description

For each base substitution type and strand the total number of mutations and the relative contribution within a group is returned.

Usage

```
strand_occurrences(mut_mat_s, by)
```

Arguments

mut_mat_s	192 feature mutation count matrix, result from 'mut_matrix_stranded()'
by	Character vector with grouping info, optional

Value

A data.frame with the total number of mutations and relative contribution within group per base substitution type and strand

See Also

[mut_matrix_stranded](#), [plot_strand](#), [plot_strand_bias](#)

Examples

```
## See the 'mut_matrix_stranded()' example for how we obtained the
## following mutation matrix.
mut_mat_s <- readRDS(system.file("states/mut_mat_s_data.rds",
                                package="MutationalPatterns"))

## Load a reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

tissue <- c("colon", "colon", "colon",
            "intestine", "intestine", "intestine",
            "liver", "liver", "liver")

strand_counts = strand_occurrences(mut_mat_s, by=tissue)
```

type_context	<i>Retrieve context of base substitution types</i>
--------------	--

Description

A function to extract the bases 3' upstream and 5' downstream of the base substitution types.

Usage

```
type_context(vcf, ref_genome)
```

Arguments

vcf	A CollapsedVCF object
ref_genome	Reference genome

Value

Mutation types and context character vectors in a named list

See Also

[read_vcfs_as_granges](#), [mut_context](#)

Examples

```
## See the 'read_vcfs_as_granges()' example for how we obtained the
## following data:
vcfs <- readRDS(system.file("states/read_vcfs_as_granges_output.rds",
                           package="MutationalPatterns"))

## Load the corresponding reference genome.
ref_genome <- "BSgenome.Hsapiens.UCSC.hg19"
library(ref_genome, character.only = TRUE)

type_context <- type_context(vcfs[[1]], ref_genome)
```

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