Package 'MutationalPatterns'

April 15, 2017

Type Package

Title Studying patterns in base substitution catalogues

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

Version 1.0.0

Date 2016-08-24

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URL https://github.com/CuppenResearch/MutationalPatterns

Imports stats, BiocGenerics (>= 0.18.0), VariantAnnotation (>= 1.18.1), reshape2 (>= 1.4.1), plyr (>= 1.8.3), ggplot2 (>= 2.1.0), pracma (>= 1.8.8), SummarizedExperiment (>= 1.2.2), IRanges (>= 2.6.0), GenomeInfoDb (>= 1.8.1), Biostrings (>= 2.40.0), gridExtra (>= 2.2.1)

Depends R (>= 3.3.0), NMF (>= 0.20.6), GenomicRanges (>= 1.24.0)

Suggests BSgenome (>= 1.40.0), BiocStyle (>= 2.0.3), biomaRt (>= 2.28.0), BSgenome.Hsapiens.UCSC.hg19 (>= 1.4.0), TxDb.Hsapiens.UCSC.hg19.knownGene (>= 3.2.2), rtracklayer (>= 1.32.2)

biocViews Genetics, SomaticMutation

ZipData NA

LazyData false

RoxygenNote 5.0.1

Encoding UTF-8

NeedsCompilation no

R topics documented:

`binomial_test` *Binomial test for enrichment or depletion testing*

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)
```

`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 genomic_distribution()
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)
```

`extract_signatures` *Extract mutational signatures from 96 mutation matrix using NMF*

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` *Find optimal nonnegative linear combination of mutation signatures to reconstruct the mutation matrix.*

Description

Find linear combination of mutation signatures that most closely reconstructs the mutation matrix by solving 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

```
## You can download the signatures from the pan-cancer study by
## Alexandrov et al:
#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)

## We should now reorder the columns to make the order of the
## trinucleotide changes the same.
cancer_signatures <- cancer_signatures[order(cancer_signatures[,1]),]

## Reduce the data set to signatures only in the matrix.
cancer_signatures <- as.matrix(cancer_signatures[,4:33])

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

## 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)
```

Arguments

vcf_list	A list with VCF GRanges objects
surveyed_list	A list with Granges of regions of the genome that have been surveyed (e.g. determined using GATK CallableLoci)
region_list	List with GRanges objects containing locations of genomic regions

Value

A data.frame containing the number observed and number of expected mutations in each genomic region.

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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal = extractSeqlevelsByGroup(species="Homo_sapiens",
                                    style="UCSC",
                                    group="auto")

vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## Use biomaRt to obtain data.
## We can query the BioMart database, but this may take a long time
## though, so we take some shortcuts by loading the results from our
## examples.  The corresponding code for downloading data can be
## found above the command we run.

# mart="ensemble"
# library(biomaRt)

# regulatory <- useEnsembl(biomart="regulation",
#                          dataset="hsapiens_regulatory_feature",
#                          GRCh = 37)
regulatory <- readRDS(system.file("states/regulatory_data.rds",
                                    package="MutationalPatterns"))

## Download the regulatory CTCF binding sites and convert them to
## a GRanges object.
# CTCF <- getBM(attributes = c('chromosome_name',
#                              'chromosome_start',
#                              'chromosome_end',
#                              'feature_type_name',
#                              'cell_type_name'),
#               filters = "regulatory_feature_type_name",
#               values = "CTCF Binding Site",
#               mart = regulatory)
#
```

```
# CTCF_g <- reduce(GRanges(CTCF$chromosome_name,
#                 IRanges(CTCF$chromosome_start,
#                 CTCF$chromosome_end)))

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

## Download the promoter regions and conver 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 <- list.files(system.file("extdata",
                            package="MutationalPatterns"),
                            pattern = ".bed",
                            full.names = TRUE)

## 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)
```

`intersect_with_region` *Find overlap between mutations and a genomic region*

Description

Find the number of mutations that reside in genomic region and take surveyed area of genome into account.

Usage

```
intersect_with_region(vcf, surveyed, region)
```

Arguments

`vcf`	CollapsedVCF object with mutations
`surveyed`	GRanges object with regions of the genome that were surveyed
`region`	GRanges object with genomic region(s)

Value

A data.frame containing the overlapping mutations for a genomic region.

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.

Author(s)

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References

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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 *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

```
mutation_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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal <- extractSeqlevelsByGroup(species="Homo_sapiens",
                                     style="UCSC",
                                     group="auto")

vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

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

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

---

mutation_types *Retrieve base substitution types from a VCF object*

Description

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

Usage

```
mutation_types(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"))

mutation_types(vcfs[[1]])
```

`mut_192_occurrences` *Count 96 trinucleotide mutation occurrences with transcriptional strand information*

Description

Count 96 trinucleotide mutation occurrences with transcriptional strand information

Usage

```
mut_192_occurrences(type_context, strand)
```

Arguments

`type_context`	result from type_context function
`strand`	character vector with strand information for each position, "U" for untranscribed, "T" for transcribed, "-" for unknown or positions outside gene bodies

Value

A vector with 192 mutation occurrences and 96 trinucleotides for both transcribed and untranscribed strand

---

`mut_96_occurrences` *Count 96 trinucleotide mutation occurrences*

Description

Count 96 trinucleotide mutation occurrences

Usage

```
mut_96_occurrences(type_context)
```

Arguments

`type_context`	result from type_context function

Value

vector with 96 trinucleotide mutation occurrences

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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal <- extractSeqlevelsByGroup(species="Homo_sapiens",
                                     style="UCSC",
                                     group="auto")

vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## 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)

## Et voila.
mut_mat
```

mut_matrix_stranded *Make mutation count matrix of 96 trinucleotides with transcriptional strand information*

Description

Make a mutation count matrix for 96 trinucleotides, for both the transcribed and untranscribed strand of gene bodies.

Usage

```
mut_matrix_stranded(vcf_list, ref_genome, genes)
```

Arguments

vcf_list	List of collapsed vcf objects
ref_genome	BSGenome reference genome object
genes	GRanges object with definition of gene bodies, including strand information

Details

Mutations outside gene bodies are not counted.

Value

192 mutation count matrix (96 * 2 strands)

See Also

read_vcfs_as_granges, link{mut_matrix}

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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal <- extractSeqlevelsByGroup(species="Homo_sapiens",
                                     style="UCSC",
                                     group="auto")

vcfs = lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

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

## You can obtain the known genes from the UCSC hg19 dataset using
## Bioconductor:
# source("https://bioconductor.org/biocLite.R")
# biocLite("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_mat_s = mut_matrix_stranded(vcfs, ref_genome, genes_hg19)
```

`mut_type_occurrences` *Count the occurrences of each base substitution type*

Description

Count the occurrences of each base substitution type

Usage

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

Arguments

`vcf_list`	A list of CollapsedVCF object
`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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal <- extractSeqlevelsByGroup(species="Homo_sapiens",
                                     style="UCSC",
                                     group="auto")

vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## 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 = 0.15)
```

Arguments

`mut_matrix`	192 trinucleotide profile matrix
`colors`	6 value color vector
`ymax`	Y axis maximum value, default = 0.015

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.
nmf_res_strand <- extract_signatures(mut_mat_s, rank = 2)

## 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 = 0.15)
```

Arguments

mut_matrix	96 trinucleotide profile matrix
colors	6 value color vector
ymax	Y axis maximum value, default = 0.015

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 = 0.15, diff_ylim = c(-0.02, 0.02), colors)
```

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 = 0.15
diff_ylim	Y-axis limits for profile difference plot, default = c(-0.02, 0.02)
colors	6 value color vector

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 orignal profile
plot_compare_profiles(mut_mat[,1],
                      nmf_res$reconstructed[,1],
                      profile_names = c("Original", "Reconstructed"))
```

---

plot_contribution *Plot signature contribution*

Description

Plot contribution of signatures

Usage

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

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"

Value

Stacked barplot with contribution of each signatures 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_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"))

## Exclude mitochondrial and autosomal chromosomes.
autosomal = extractSeqlevelsByGroup(species="Homo_sapiens",
                                    style="UCSC",
                                    group="auto")
```

```
vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

# Take the 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` *Plot point mutation spectrum*

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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal = extractSeqlevelsByGroup(species="Homo_sapiens",
                                    style="UCSC",
                                    group="auto")

vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## 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*

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_bias(strand_bias, colors)
```

Arguments

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

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 a seqlevel style to the GRanges objects. The default seqlevel style is "UCSC".

Usage

```
read_vcfs_as_granges(vcf_files, sample_names, genome = "-", style = "UCSC")
```

Arguments

vcf_files	Character vector of vcf file names
sample_names	Character vector of sample names
genome	A character or Seqinfo object
style	The naming standard to use for the GRanges. (default = "UCSC")

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)

# This function loads the files as GRanges objects
vcfs <- read_vcfs_as_granges(vcf_files, sample_names, genome = "hg19")
```

`strand_bias_test` *Significance test for transcriptional strand asymmetry*

Description

This function performs a Poisson test for the ratio between mutations on the transcribed and untranscribed 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 transcribed and untrascribed strand 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` *Find transcriptional strand of base substitutions in vcf*

Description

For the positions 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.)

Usage

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

Arguments

`vcf`	GRanges containing the VCF object
`genes`	GRanges with gene bodies definitions including strand information

Details

Base substitions 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.

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"))

# Exclude mitochondrial and allosomal chromosomes.
autosomal = extractSeqlevelsByGroup(species="Homo_sapiens",
                                    style="UCSC",
                                    group="auto")

vcfs = lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## You can obtain the known genes from the UCSC hg19 dataset using
## Bioconductor:
# source("https://bioconductor.org/biocLite.R")
# biocLite("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"))

strand_from_vcf(vcfs[[1]], genes_hg19)
```

---

strand_occurrences *Count occurrences per base substitution type and transcriptional strand*

Description

For each base substitution type and transcriptional 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 transcriptional strand (T = transcribed strand, U = untranscribed 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` *Retrieve context of base substitution types*

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`, `mutation_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"))

## Exclude mitochondrial and allosomal chromosomes.
autosomal <- extractSeqlevelsByGroup(species="Homo_sapiens",
                                     style="UCSC",
                                     group="auto")
```

```
vcfs <- lapply(vcfs, function(x) keepSeqlevels(x, autosomal))

## 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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