Package ‘sigminer’

June 30, 2022

Title Extract, Analyze and Visualize Mutational Signatures for Genomic Variations

Version 2.1.5

Description Genomic alterations including single nucleotide substitution, copy number alteration, etc. are the major force for cancer initialization and development. Due to the specificity of molecular lesions caused by genomic alterations, we can generate characteristic alteration spectra, called 'signature' (Wang, Shixiang, et al. (2021) <DOI:10.1371/journal.pgen.1009557> & Alexandrov, Ludmil B., et al. (2020) <DOI:10.1038/s41586-020-1943-3> & Steele Christopher D., et al. (2022) <DOI:10.1038/s41586-022-04738-6>). This package helps users to extract, analyze and visualize signatures from genomic alteration records, thus providing new insight into cancer study.

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URL https://github.com/ShixiangWang/sigminer

BugReports https://github.com/ShixiangWang/sigminer/issues

Depends R (>= 3.5)

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Author  Shixiang Wang [aut, cre] (<https://orcid.org/0000-0001-9855-7357>),
        Ziyu Tao [aut] (<https://orcid.org/0000-0003-3272-1227>),
        Huimin Li [aut] (<https://orcid.org/0000-0003-1683-9057>),
        Tao Wu [aut] (<https://orcid.org/0000-0002-8999-9628>),
        Xue-Song Liu [aut, ctb] (<https://orcid.org/0000-0002-7736-0077>),
        Anand Mayakonda [ctb]

Maintainer  Shixiang Wang <w_shixiang@163.com>
Repository  CRAN
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add_h_arrow

Add Horizontal Arrow with Text Label to a ggplot

Description

Add Horizontal Arrow with Text Label to a ggplot

Usage

```
add_h_arrow(
  p,
  x,
  y,
  label = "optimal number",
  space = 0.01,
  vjust = 0.3,
  seg_len = 0.1,
  arrow_len = unit(2, "mm"),
  arrow_type = c("closed", "open"),
  font_size = 5,
  font_family = c("serif", "sans", "mono"),
  font_face = c("plain", "bold", "italic")
)
```
add_labels

Arguments

- **p**: a ggplot.
- **x**: position at x axis.
- **y**: position at y axis.
- **label**: text label.
- **space**: a small space between arrow and text.
- **vjust**: vertical adjustment, set to 0 to align with the bottom, 0.5 for the middle, and 1 (the default) for the top.
- **seg_len**: length of the arrow segment.
- **arrow_len**: length of the arrow.
- **arrow_type**: type of the arrow.
- **font_size**: font size.
- **font_family**: font family.
- **font_face**: font face.

Value

- a ggplot object.

Description

Add text labels to a ggplot object, such as the result from `show_sig_profile`.

Usage

```r
add_labels(
  p,
  x, y,
  y_end = NULL,
  n_label = NULL,
  labels = NULL,
  revert_order = FALSE,
  font_size = 5,
  font_family = "serif",
  font_face = c("plain", "bold", "italic"),
  ...)
```
add_labels

Arguments

p  a ggplot.
x  position at x axis.
y  position at y axis.
y_end  end position of y axis when n_label is set.
n_label  the number of label, when this is set, the position of labels at y axis is auto-generated according to y and y_end.
labels  text labels or a similarity object from get_sig_similarity.
revert_order  if TRUE, revert label order.
font_size  font size.
font_family  font family.
font_face  font face.
...  other parameters passing to ggplot2::annotate.

Value

a ggplot object.

Examples

# Load mutational signature
load(system.file("extdata", "toy_mutational_signature.RData", package = "sigminer", mustWork = TRUE))

# Show signature profile
p <- show_sig_profile(sig2, mode = "SBS")

# Method 1
p1 <- add_labels(p,
  x = 0.75, y = 0.3, y_end = 0.9, n_label = 3,
  labels = paste0("text", 1:3)
)
p1

# Method 2
p2 <- add_labels(p,
  x = c(0.15, 0.6, 0.75), y = c(0.3, 0.6, 0.9),
  labels = paste0("text", 1:3)
)
p2

# Method 3
sim <- get_sig_similarity(sig2)
p3 <- add_labels(p,
  x = c(0.15, 0.6, 0.75), y = c(0.25, 0.55, 0.8),
  labels = sim, font_size = 2)
p3
A Best Practice for Signature Extraction and Exposure (Activity) Attribution

Description

These functions are combined to provide a best practice for optimally identifying mutational signatures and attributing their activities (exposures) in tumor samples. They are listed in order to use.

- `bp_extract_signatures()` for extracting signatures.
- `bp_show_survey()` for showing measures change under different signature numbers to help user select optimal signature number. At default, an aggregated score (named score) is generated to suggest the best solution.
- `bp_show_survey2()` for showing simplified signature number survey like `show_sig_number_survey()`.
- `bp_get_sig_obj()` for get a (list of) Signature object which is common used in `sigminer` for analysis and visualization.
- `bp_attribute_activity()` for optimizing signature activities (exposures). NOTE: the activities from extraction step may be better! You can also use `sig_extract` to get optimal NMF result from multiple NMF runs. Besides, you can use `sig_fit` to quantify exposures based on signatures extracted from `bp_extract_signatures()`.
- `bp_extract_signatures_iter()` for extracting signature in a iteration way.
- `bp_cluster_iter_list()` for clustering (hclust with average linkage) iterated signatures to help collapse multiple signatures into one. The result cluster can be visualized by `plot()` or `factoextra::fviz_dend()`.
- `bp_get_clustered_sigs()` for getting clustered (grouped) mean signatures from signature clusters.
- Extra: `bp_get_stats()` for obtaining stats for signatures and samples of a solution. These stats are aggregated (averaged) as the stats for a solution (specific signature number).
- Extra: `bp_get_rank_score()` for obtaining rank score for all signature numbers.

Usage

```r
bp_extract_signatures(
  nmf_matrix,
  range = 2:5,
  n_bootstrap = 20L,
  n_nmf_run = 50,
  RTOL = 0.001,
  min_contribution = 0,
  cores = min(4L, future::availableCores()),
  cores_solution = min(cores, length(range)),
  seed = 123456L,
  handle_hyper_mutation = TRUE,
)```
bp_extract_signatures_iter(
  nmf_matrix,
  range = 2:5,
  sim_threshold = 0.95,
  max_iter = 10L,
  n_bootstrap = 20L,
  n_nmf_run = 50,
  RTOL = 0.001,
  min_contribution = 0,
  cores = min(4L, future::availableCores()),
  cores_solution = min(cores, length(range)),
  seed = 123456L,
  handle_hyper_mutation = TRUE,
  report_integer_exposure = FALSE,
  only_core_stats = nrow(nmf_matrix) > 100,
  cache_dir = file.path(tempdir(), "sigminer_bp"),
  keep_cache = FALSE,
  pymmf = FALSE,
  use_conda = TRUE,
  py_path = "/Users/wsx/anaconda3/bin/python"
)

bp_cluster_iter_list(x, k = NULL, include_final_iteration = TRUE)

bp_get_clustered_sigs(SigClusters, cluster_label)

bp_get_sig_obj(obj, signum = NULL)

bp_get_stats(obj)

bp_get_rank_score(obj)

bp_show_survey2(
  obj,
  x = "signature_number",
  left_y = "silhouette",
  right_y = "L2_error",
  left_name = left_y,
  right_name = right_y,
left_color = "black",
right_color = "red",
left_shape = 16,
right_shape = 18,
shape_size = 4,
highlight = NULL
)

bp_show_survey(
  obj,
  add_score = FALSE,
  scales = c("free_y", "free"),
  fixed_ratio = TRUE
)

bp_attribute_activity(
  input,
  sample_class = NULL,
  nmf_matrix = NULL,
  method = c("bt", "stepwise"),
  bt_use_prop = FALSE,
  return_class = c("matrix", "data.table"),
  use_parallel = FALSE,
  cache_dir = file.path(tempdir(), "sigminer_attribute_activity"),
  keep_cache = FALSE
)

Arguments

nmf_matrix a matrix used for NMF decomposition with rows indicate samples and columns indicate components.

range a numeric vector containing the ranks of factorization to try. Note that duplicates are removed and values are sorted in increasing order. The results are notably returned in this order.

n_bootstrap number of bootstrapped (resampling) catalogs used. When it is 0, the original (input) mutation catalog is used for NMF decomposition, this is not recommended, just for testing, user should not set it to 0.

n_nmf_run number of NMF runs for each bootstrapped or original catalog. At default, in total n_bootstrap x n_nmf_run (i.e. 1000) NMF runs are used for the task.

RTOL a threshold proposed by Nature Cancer paper to control how to filter solutions of NMF. Default is 0.1% (from reference #2), only NMF solutions with KLD (KL deviance) <= 100.1% minimal KLD are kept.

min_contribution a component contribution threshold to filter out small contributed components.

cores number of cpu cores to run NMF.
cores_solution cores for processing solutions, default is equal to argument cores.
seed a random seed to make reproducible result.
handle_hyper_mutation
default is TRUE, handle hyper-mutant samples.

report_integer_exposure
if TRUE, report integer signature exposure by bootstrapping technique.

only_core_stats
if TRUE, only calculate the core stats for signatures and samples.

cache_dir
a directory for keep temp result files.

keep_cache
if TRUE, keep cache results.

pynmf
if TRUE, use Python NMF driver Nimfa. The seed currently is not used by this implementation, so the only way to reproduce your result is setting keep_cache = TRUE.

use_conda
if TRUE, create an independent conda environment to run NMF.

py_path
path to Python executable file, e.g. '/Users/wsx/anaconda3/bin/python'. In my test, it is more stable than use_conda=TRUE. You can install the Nimfa package by yourself or set use_conda to TRUE to install required Python environment, and then set this option.

sim_threshold
a similarity threshold for selecting samples to auto-rerun the extraction procedure (i.e. bp_extract_signatures()), default is 0.95.

max_iter
the maximum iteration size, default is 10, i.e., at most run the extraction procedure 10 times.

x
result from bp_extract_signatures_iter() or a list of Signature objects.

k
an integer sequence specifying the cluster number to get silhouette.

include_final_iteration
if FALSE, exclude final iteration result from clustering for input from bp_extract_signatures_iter(), not applied if input is a list of Signature objects.

SigClusters
result from bp_cluster_iter_list().

cluster_label
cluster labels for a specified cluster number, obtain it from SigClusters$sil_df.

obj
a ExtractionResult object from bp_extract_signatures().

signum
a integer vector to extract the corresponding Signature object(s). If it is NULL (default), all will be returned.

left_y
column name for left y axis.

right_y
column name for right y axis.

left_name
label name for left y axis.

right_name
label name for right y axis.

left_color
color for left axis.

right_color
color for right axis.

left_shape, right_shape, shape_size
shape setting.

highlight
a integer to highlight a x.

add_score
if FALSE, don’t show score and label optimal points by rank score.

scales
one of "free_y" (default) and "free" to control the scales of plot facet.
fixed_ratio  if TRUE (default), make the x/y axis ratio fixed.
input  result from bp_extract_signatures() or a Signature object.
sample_class  a named string vector whose names are sample names and values are class labels (i.e. cancer subtype). If it is NULL (the default), treat all samples as one group.
method  one of 'bt' (use bootstrap exposure median, from reference #2, the most recommended way in my personal view) or stepwise' (stepwise reduce and update signatures then do signature fitting with last signature sets, from reference #2, the result tends to assign the contribution of removed signatures to the remaining signatures, maybe I misunderstand the paper method? PAY ATTENTION).
bתכUseProp  this parameter is only used for bt method to reset low contributing signature activity (relative activity <0.01). If TRUE, use empirical P value calculation way (i.e. proportion, used by reference #2), otherwise a t.test is applied.
return_class  string, 'matrix' or 'data.table'.
use_parallel  if TRUE, use parallel computation based on furrr package. It can also be an integer for specifying cores.

Details

The signature extraction approach is adopted from reference #1, #2, and the whole best practice is adopted from the pipeline used by reference #3. I implement the whole procedure with R code based on the method description of papers. The code is well organized, tested and documented so user will find it pretty simple and useful. Besides, the structure of the results is very clear to see and also visualize like other approaches provided by sigminer.

Value

It depends on the called function.

Measure Explanation in Survey Plot

The survey plot provides a pretty good way to facilitate the signature number selection. A score measure is calculated as the weighted mean of selected measures and visualized as the first sub-plot. The optimal number is highlighted with red color dot and the best values for each measures are also highlighted with orange color dots. The detail of 6 measures shown in plot are explained as below.

- score - an aggregated score based on rank scores from selected measures below. The higher, the better. When two signature numbers have the same score, the larger signature number is preferred (this is a rare situation, you have to double check other measures).
- silhouette - the average silhouette width for signatures, also named as ASW in reference #2. The signature number with silhouette decreases sharply is preferred.
- distance - the average sample reconstructed cosine distance, the lower value is better.
- error - the average sample reconstructed error calculated with L2 formula (i.e. L2 error). This lower value is better. This measure represents a similar concept like distance above, they are all used to quantify how well sample mutation profiles can be reconstructed from signatures, but distance cares the whole mutation profile similarity while error here cares value difference.
• pos cor - the average positive signature exposure correlation coefficient. The lower value is better. This measure is constructed based on my understanding about signatures: mutational signatures are typically treated as independent recurrent patterns, so their activities are less correlated.

• similarity - the average similarity within in a signature cluster. Like silhouette, the point decreases sharply is preferred. In the practice, results from multiple NMF runs are clustered with "clustering with match" algorithm proposed by reference #2. This value indicates if the signature profiles extracted from different NMF runs are similar.

Author(s)

Shixiang Wang w_shixiang@163.com

References


See Also

See sig_estimate, sig_extract, sig_auto_extract, sigprofiler_extract for other approaches.

Examples

data("simulated_catalogs")

# Here I reduce the values for n_bootstrap and n_nmf_run
# for reducing the run time.
# In practice, you should keep default or increase the values
# for better estimation.
#
# The input data here is simulated from 10 mutational signatures
#
# e1 <- bp_extract_signatures(
# t(simulated_catalogs$set1),
# range = 8:12,
# n_bootstrap = 5,
# n_nmf_run = 10
# )
#
# To avoid computation in examples,
# Here just load the result
# (e1$signature and e1$exposure set to NA to reduce package size)
load(system.file("extdata", "e1.RData", package = "sigminer"))
# See the survey for different signature numbers
# The suggested solution is marked as red dot
# with highest integrated score.
p1 <- bp_show_survey(e1)
p1

# You can also exclude plotting and highlighting the score
p2 <- bp_show_survey(e1, add_score = FALSE)
p2

# You can also plot a simplified version
p3 <- bp_show_survey2(e1, highlight = 10)
p3

# Obtain the suggested solution from extraction result
obj_suggested <- bp_get_sig_obj(e1, e1$suggested)
obj_suggested

# If you think the suggested signature number is not right
# Just pick up the solution you want
obj_s8 <- bp_get_sig_obj(e1, 8)

# Track the reconstructed profile similarity
rec_sim <- get_sig_rec_similarity(obj_s8, t(simulated_catalogs$set1))
rec_sim

# After extraction, you can assign the signatures
# to reference COSMIC signatures
# More see ?get_sig_similarity
sim <- get_sig_similarity(obj_suggested)

# Visualize the match result
if (require(pheatmap)) {
  pheatmap::pheatmap(sim$similarity)
}

# You already got the activities of signatures
# in obj_suggested, however, you can still
# try to optimize the result.
# NOTE: the optimization step may not truly optimize the result!
expo <- bp_attribute_activity(e1, return_class = "data.table")
expo$abs_activity

## Not run:
# Iterative extraction:
# This procedure will rerun extraction step
# for those samples with reconstructed catalog similarity
# lower than a threshold (default is 0.95)
e2 <- bp_extract_signatures_iter(
  t(simulated_catalogs$set1),
  range = 9:11,
  n_bootstrap = 5,
  n_nmf_run = 5,
  sim_threshold = 0.99
)
When the procedure run multiple rounds
# you can cluster the signatures from different rounds by
# the following command
# bp_cluster_iter_list(e2)

## Extra utilities
rank_score <- bp_get_rank_score(e1)
risk_score
stats <- bp_get_stats(e2$iter1)
# Get the mean reconstructed similarity
1 - stats$stats_sample$cosine_distance_mean

## End(Not run)

centromeres.hg19

Location of Centromeres at Genome Build hg19

Description
Location of Centromeres at Genome Build hg19

Format
A data.frame

Source
Generate from UCSC gold path

Examples
data(centromeres.hg19)

centromeres.hg38

Location of Centromeres at Genome Build hg38

Description
Location of Centromeres at Genome Build hg38

Format
A data.frame

Source
Generate from Genome Reference Consortium
examples

data(centromeres.hg38)

centromeres.mm10  Location of Centromeres at Genome Build mm10

Description
Location of Centromeres at Genome Build mm10

Format
A data.frame

Source
Generate from https://hgdownload.soe.ucsc.edu/goldenPath/mm10/database/gap.txt.gz

examples
data(centromeres.mm10)

centromeres.mm9  Location of Centromeres at Genome Build mm9

Description
Location of Centromeres at Genome Build mm9

Format
A data.frame

Source
Generate from https://hgdownload.soe.ucsc.edu/goldenPath/mm9/database/ with code:

for i in $(seq 1 19) X Y;
do
wget https://hgdownload.soe.ucsc.edu/goldenPath/mm9/database/chr$i_gap.txt.gz
done

Examples
data(centromeres.mm9)
**chromsize.hg19**  
*Chromosome Size of Genome Build hg19*

**Description**  
Chromosome Size of Genome Build hg19

**Format**  
A data.frame

**Source**  
Generate from UCSC gold path

**Examples**  
```
data(chromsize.hg19)
```

**chromsize.hg38**  
*Chromosome Size of Genome Build hg38*

**Description**  
Chromosome Size of Genome Build hg38

**Format**  
A data.frame

**Source**  
Generate from UCSC gold path

**Examples**  
```
data(chromsize.hg38)
```
chromsize.mm10  

**Chromosome Size of Genome Build mm10**

**Description**

Chromosome Size of Genome Build mm10

**Format**

A data.frame

**Source**

Generate from UCSC gold path [http://hgdownload.cse.ucsc.edu/goldenPath/mm10/bigZips/mm10.chrom.sizes](http://hgdownload.cse.ucsc.edu/goldenPath/mm10/bigZips/mm10.chrom.sizes)

**Examples**

```r
data(chromsize.mm10)
```

---

chromsize.mm9  

**Chromosome Size of Genome Build mm9**

**Description**

Chromosome Size of Genome Build mm9

**Format**

A data.frame

**Source**

Generate from UCSC gold path [http://hgdownload.cse.ucsc.edu/goldenPath/mm9/bigZips/mm9.chrom.sizes](http://hgdownload.cse.ucsc.edu/goldenPath/mm9/bigZips/mm9.chrom.sizes)

**Examples**

```r
data(chromsize.mm9)
```
## CopyNumber-class

### Description

Classification Table of Copy Number Features Devised by Wang et al. for Method 'W'

### Format

A data.table with "sigminer.features" class name

### Source

Generate from code under data_raw/

### Examples

```r
data(CN.features)
```

### CopyNumber-class

#### Description

S4 class for storing summarized absolute copy number profile.

#### Slots

- `data` : data.table of absolute copy number calling.
- `summary.per.sample` : data.table of copy number variation summary per sample.
- `genome_build` : genome build version, should be one of 'hg19' or 'hg38'.
- `genome_measure` : Set 'called' will use autosomo called segments size to compute total size for CNA burden calculation, this option is useful for WES and target sequencing. Set 'wg' will autosome size from genome build, this option is useful for WGS, SNP etc..
- `annotation` : data.table of annotation for copy number segments.
- `dropoff.segs` : data.table of copy number segments dropped from raw input.
cosine

Calculate Cosine Measures

Description

Calculate Cosine Measures

Usage

cosine(x, y)

Arguments

x  
a numeric vector or matrix with column representing vector to calculate similarity.
y  
must be same format as x.

Value

a numeric value or matrix.

Examples

x <- c(1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0)
y <- c(0, 0, 1, 1, 1, 1, 1, 0, 1, 0, 0, 0)
z1 <- cosine(x, y)
z1
z2 <- cosine(matrix(x), matrix(y))
z2

cytobands.hg19

Location of Chromosome Cytobands at Genome Build hg19

Description

Location of Chromosome Cytobands at Genome Build hg19

Format

A data.frame

Source

from UCSC

Examples

data(cytobands.hg19)
cytobands.hg38  
Location of Chromosome Cytobands at Genome Build hg38

Description
Location of Chromosome Cytobands at Genome Build hg38

Format
A data.frame

Source
from UCSC

Examples

data(cytobands.hg38)

---

cytobands.mm10  
Location of Chromosome Cytobands at Genome Build mm10

Description
Location of Chromosome Cytobands at Genome Build mm10

Format
A data.frame

Source
from UCSC http://hgdownload.cse.ucsc.edu/goldenpath/mm10/database/cytoBand.txt.gz

Examples

data(cytobands.mm10)
cytobands.mm9  Location of Chromosome Cytobands at Genome Build mm9

description
Location of Chromosome Cytobands at Genome Build mm9

format
A data.frame

source
from UCSC http://hgdownload.cse.ucsc.edu/goldenpath/mm9/database/cytoBand.txt.gz

examples
data(cytobands.mm9)

enrich_component_strand_bias
Performs Strand Bias Enrichment Analysis for a Given Sample-by-Component Matrix

description
See sig_tally for examples.

usage
enrich_component_strand_bias(mat)

arguments
mat a sample-by-component matrix from sig_tally with strand bias labels "T:" and "B:.

value
a data.table sorted by p_value.
get_adj_p

Get Adjust P Values from Group Comparison

Description

Setting `aes(label=..p.adj..)` in `ggpubr::compare_means()` does not show adjust p values. The returned result of this function can be combined with `ggpubr::stat_pvalue_manual()` to fix this problem.

Usage

```r
get_adj_p(
  data, 
  .col, 
  .grp = "Sample", 
  comparisons = NULL, 
  method = "wilcox.test", 
  p.adjust.method = "fdr", 
  p.digits = 3L, 
  ...
)
```

Arguments

- `data`: a `data.frame` containing column for groups and column for comparison.
- `col`: column name for comparison.
- `grp`: column name for groups.
- `comparisons`: Default is `NULL`, use all combination in group column. It can be a list of length-2 vectors. The entries in the vector are either the names of 2 values on the x-axis or the 2 integers that correspond to the index of the groups of interest, to be compared.
- `method`: a character string indicating which method to be used for comparing means. It can be 't.test', 'wilcox.test' etc..
- `p.adjust.method`: correction method, default is 'fdr'. Run `p.adjust.methods` to see all available options.
- `p.digits`: how many significant digits are to be used.
- `...`: other arguments passed to `ggpubr::compare_means()`

Details

More info see `ggpubr::compare_means()`, `ggpubr::stat_compare_means()` and `stats::p.adjust()`.

Value

a `data.frame` containing comparison result
get_Aneuploidy_score

Get Aneuploidy Score from Copy Number Profile

Source

https://github.com/kassambara/ggpubr/issues/143

Examples

library(ggpubr)
# T-test
stat.test <- compare_means(
  len ~ dose,
  data = ToothGrowth,
  method = "t.test",
  p.adjust.method = "fdr"
)
stat.test

# Create a simple box plot
p <- ggboxplot(ToothGrowth, x = "dose", y = "len")
p

# Add p values
my_comparisons <- list(c("0.5", "1"), c("1", "2"), c("0.5", "2"))
p + stat_compare_means(method = "t.test", comparisons = my_comparisons)

# Try adding adjust p values
# proposed by author of ggpubr
# however it does not work
p + stat_compare_means(aes(label = ..p.adj..), method = "t.test", comparisons = my_comparisons)

# Solution:
# calculate adjust p values and their location
# then use stat_pvalue_manual() function
p_adj <- get_adj_p(ToothGrowth, .col = "len", .grp = "dose")
p_adj
p + stat_pvalue_manual(p_adj, label = "p.adj")

# Show selected comparisons
# Of note, p value is adjusted
# for three comparisons, but only
# two are showed in figure
p_adj <- get_adj_p(ToothGrowth,
  .col = "len", .grp = "dose",
  comparisons = list(c("0.5", "1"), c("1", "2")))
p + stat_pvalue_manual(p_adj, label = "p.adj")
Description

This implements a Cohen-Sharir method (see reference) like "Aneuploidy Score" computation. You can read the source code to see how it works. Basically, it follows the logic of Cohen-Sharir method but with some difference in detail implementation. Their results should be counterpart, but with no data validation for now. Please raise an issue if you find problem/bugs in this function.

Usage

```r
get_Aneuploidy_score(
    data,
    ploidy_df = NULL,
    genome_build = "hg19",
    rm_black_arms = FALSE
)
```

Arguments

- `data`: a CopyNumber object or a `data.frame` containing at least 'chromosome', 'start', 'end', 'segVal', 'sample' these columns.
- `ploidy_df`: default is NULL, compute ploidy by segment-size weighted copy number across autosome, see `get_cn_ploidy`. You can also provide a `data.frame` with 'sample' and 'ploidy' columns.
- `genome_build`: genome build version, should be 'hg19', 'hg38', 'mm9' or 'mm10'.
- `rm_black_arms`: if TRUE, remove short arms of chr13/14/15/21/22 from calculation as documented in reference #3.

Value

A `data.frame`

References

- Logic reference: [https://github.com/queue2/aneuploidy_score/](https://github.com/queue2/aneuploidy_score/).

Examples

```r
# Load copy number object
load(system.file("extdata", "toy_copynumber.RData",
    package = "sigminer", mustWork = TRUE
))

df <- get_Aneuploidy_score(cn)
df
```
get_bayesian_result

Description

Sometimes, we may want to use or inspect specified run result from `sig_auto_extract`. This function is designed for this purpose.

Usage

get_bayesian_result(run_info)

Arguments

run_info a data.frame with 1 row and two necessary columns Run and file.

Value

alist.

Author(s)

Shixiang Wang

Examples

```r
load(system.file("extdata", "toy_copynumber_tally_W.RData", 
  package = "sigminer", mustWork = TRUE 
))

res <- sig_auto_extract(cn_tally_W$nmf_matrix, result_prefix = "Test_copynumber", nrun = 1)
# All run info are stored in res$Raw$summary_run
# Obtain result of run 1
res_run1 <- get_bayesian_result(res$Raw$summary_run[1, ])
```
**get_cn_freq_table**  
*Get CNV Frequency Table*

**Description**
Get CNV Frequency Table

**Usage**
```r
get_cn_freq_table(
  data,
  genome_build = "hg19",
  cutoff = 2L,
  resolution_factor = 1L
)
```

**Arguments**
- **data**: a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal', 'sample' these columns.
- **genome_build**: genome build version, used when data is a data.frame, should be 'hg19' or 'hg38'.
- **cutoff**: copy number value cutoff for splitting data into AMP and DEL. The values equal to cutoff are discarded. Default is 2, you can also set a length-2 vector, e.g. c(2, 2).
- **resolution_factor**: an integer to control the resolution. When it is 1 (default), compute frequency in each cytoband. When it is 2, use compute frequency in each half cytoband.

**Value**
a data.table.

---

**get_cn_ploidy**  
*Get Ploidy from Absolute Copy Number Profile*

**Description**
Get Ploidy from Absolute Copy Number Profile

**Usage**
```r
get_cn_ploidy(data)
```
get_genome_annotation

Arguments

data a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal' these columns.

Value

a value or a data.table

Examples

# Load copy number object
load(system.file("extdata", "toy_copynumber.RData", 
 package = "sigminer", mustWork = TRUE 
))

df <- get_cn_ploidy(cn)
df

get_genome_annotation  Get Genome Annotation

Description

Get Genome Annotation

Usage

get_genome_annotation(
  data_type = c("chr_size", "centro_loc", "cytobands", "transcript"),
  chrs = paste0("chr", c(1:22, "X", "Y")),
  genome_build = c("hg19", "hg38", "mm10", "mm9")
)

Arguments

data_type 'chr_size' for chromosome size, 'centro_loc' for location of centromeres, 'cytobands' for location of chromosome cytobands and 'transcript' for location of transcripts.

chrs chromosomes start with 'chr'

genome_build one of 'hg19', 'hg38'

Value

a data.frame containing annotation data
**get_groups**

*Get Sample Groups from Signature Decomposition Information*

**Description**

One of key results from signature analysis is to cluster samples into different groups. This function takes `Signature` object as input and return the membership in each cluster.

**Usage**

```r
get_groups(
  Signature,
  method = c("consensus", "k-means", "exposure", "samples"),
  n_cluster = NULL,
  match_consensus = TRUE
)
```

**Arguments**

- **Signature**: a `Signature` object obtained either from `sig_extract` or `sig_auto_extract`. Now it can be used to relative exposure result in `data.table` format from `sig_fit`.
- **method**: grouping method, more see details, could be one of the following:
  - 'consensus' - returns the cluster membership based on the hierarchical clustering of the consensus matrix, it can only be used for the result obtained by `sig_extract()` with multiple runs using `NMF` package.
  - 'k-means' - returns the clusters by k-means.
  - 'exposure' - assigns a sample into a group whose signature exposure is dominant.

**Examples**

```r
df1 <- get_genome_annotation()
df1
df2 <- get_genome_annotation(genome_build = "hg38")
df2
df3 <- get_genome_annotation(data_type = "centro_loc")
df3
df4 <- get_genome_annotation(data_type = "centro_loc", genome_build = "hg38")
df4
df5 <- get_genome_annotation(data_type = "cytobands")
df5
df6 <- get_genome_annotation(data_type = "cytobands", genome_build = "hg38")
df6
```
get_groups

- 'samples' - returns the cluster membership based on the contribution of signature to each sample, it can only be used for the result obtained by `sig_extract()` using NMF package.

n_cluster only used when the method is 'k-means'.

match_consensus only used when the method is 'consensus'. If TRUE, the result will match order as shown in consensus map.

Details

Users may find there are bigger differences between using method 'samples' and 'exposure' but they use a similar idea to find dominant signature, here goes the reason:

Method 'samples' using data directly from NMF decomposition, this means the two matrix $W$ (basis matrix or signature matrix) and $H$ (coefficient matrix or exposure matrix) are the results of NMF. For method 'exposure', it uses the signature exposure loading matrix. In this situation, each signature represents a number of mutations (alterations) about implementation please see source code of `sig_extract()` function.

Value

a data.table object

See Also

`NMF::predict()`, `show_groups`.

Examples

```r
# Load copy number prepare object
load(system.file("extdata", "toy_copynumber_tally_W.RData", package = "sigminer", mustWork = TRUE ))
# Extract copy number signatures
library(NMF)
sig <- sig_extract(cn_tally_W$nmf_matrix, 2, nrun = 10 )

# Methods 'consensus' and 'samples' are from NMF::predict()
g1 <- get_groups(sig, method = "consensus", match_consensus = TRUE)
g1
g2 <- get_groups(sig, method = "samples")
g2

# Use k-means clustering
g3 <- get_groups(sig, method = "k-means")
g3
```
get_group_comparison  
Get Comparison Result between Signature Groups

Description

Compare genotypes/phenotypes based on signature groups (samples are assigned to several groups). For categorical type, calculate fisher p value (using stats::fisher.test) and count table. In larger than 2 by 2 tables, compute p-values by Monte Carlo simulation. For continuous type, calculate anova p value (using stats::aov), summary table and Tukey Honest significant difference (using stats::TukeyHSD). The result of this function can be plotted by show_group_comparison().

Usage

group_comparison(  
data,  
col_group,  
cols_to_compare,  
type = "ca",  
NAs = NA,  
verbose = FALSE
)

Arguments

data  
a data.frame containing signature groups and genotypes/phenotypes (including categorical and continuous type data) want to analyze. User need to construct this data.frame by him/herself.

col_group  
column name of signature groups.

cols_to_compare  
column names of genotypes/phenotypes want to summarize based on groups.

type  
a character vector with length same as cols_to_compare, ’ca’ for categorical type and ’co’ for continuous type.

NAs  
default is NA, filter NAs for categorical columns. Otherwise a value (either length 1 or length same as cols_to_compare) fill NAs.

verbose  
if TRUE, print extra information.

Value

A list contains data, summary, p value etc..

Author(s)

Shixiang Wang w_shixiang@163.com
Examples

```r
load(system.file("extdata", "toy_copynumber_signature_by_W.RData", package = "sigminer", mustWork = TRUE ))

# Assign samples to clusters
groups <- get_groups(sig, method = "k-means")

set.seed(1234)

groups$prob <- rnorm(10)
groups$new_group <- sample(c("1", "2", "3", "4", NA), size = nrow(groups), replace = TRUE)

# Compare groups (filter NAs for categorical columns)
groups.cmp <- get_group_comparison(groups[, -1],
  col_group = "group",
  cols_to_compare = c("prob", "new_group"),
  type = c("co", "ca"), verbose = TRUE )

# Compare groups (Set NAs of categorical columns to 'Rest')
groups.cmp2 <- get_group_comparison(groups[, -1],
  col_group = "group",
  cols_to_compare = c("prob", "new_group"),
  type = c("co", "ca"), NAs = "Rest", verbose = TRUE )
```

---

### get_intersect_size

**Get Overlap Size between Interval x and y**

**Description**

Get Overlap Size between Interval x and y

**Usage**

```r
get_intersect_size(x.start, x.end, y.start, y.end)
```

**Arguments**

- `x.start`: start position of interval x.
- `x.end`: start position of interval x.
- `y.start`: start position of interval x.
- `y.end`: start position of interval x.
get_pLOH_score

Value

a numeric vector.

Examples

```r
o1 <- get_intersect_size(1, 5, 3, 20)
o1
o2 <- get_intersect_size(3, 20, 1, 10)
o2
o3 <- get_intersect_size(c(1, 2, 1), c(10, 4, 6), c(4, 2, 5), c(10, 3, 22))
o3
```

Description

pLOH score represents the genome that displayed LOH.

Usage

```r
get_pLOH_score(data, rm_chrs = c("chrX", "chrY"), genome_build = "hg19")
```

Arguments

- `data`: a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal', 'minor_cn', 'sample' these columns.
- `rm_chrs`: chromosomes to be removed in calculation. Default is sex chromosomes (recommended).
- `genome_build`: genome build version, should be 'hg19', 'hg38', 'mm9' or 'mm10'.

Value

A data.frame

References

get_shannon_diversity_index

Examples

# Load toy dataset of absolute copynumber profile
load(system.file("extdata", "toy_segTab.RData",
    package = "sigminer", mustWork = TRUE))

set.seed(1234)
segTabs$minor_cn <- sample(c(0, 1), size = nrow(segTabs), replace = TRUE)
cn <- read_copynumber(segTabs,
    seg_cols = c("chromosome", "start", "end", "segVal"),
    genome_measure = "wg", complement = TRUE, add_loh = TRUE)

df <- get_pLOH_score(cn)
df

df2 <- get_pLOH_score(cn@data)
df2

get_shannon_diversity_index

Get Shannon Diversity Index for Signatures

Description

\[ H = - \sum_{i=1}^{n} p_i \ln(p_i) \]

where \( n \) is the number of signatures identified in the signature with exposure > cutoff, and \( p_i \) is the normalized exposure of the \( i \)th signature with exposure > cutoff. Exposures of signatures were normalized to sum to 1.

Usage

get_shannon_diversity_index(rel_expo, cutoff = 0.001)

Arguments

rel_expo a data.frame with numeric columns indicating relative signature exposures for each sample. Typically this data can be obtained from get_sig_exposure().
cutoff a relative exposure cutoff for filtering signatures, default is 0.1%.

Value

a data.frame
get_sig_cancer_type_index

Obtain Signature Index for Cancer Types

Description

Obtain Signature Index for Cancer Types

Usage

get_sig_cancer_type_index(
  sig_type = c("legacy", "SBS", "DBS", "ID"),
  seq_type = c("WGS", "WES"),
  source = c("PCAWG", "TCGA", "nonPCAWG"),
  keyword = NULL
)

Arguments

sig_type  signature type.
seq_type  sequencing type.
source    data source.
keyword   keyword to search in the signature index database.

Value

a list.
get_sig_db

Examples

```r
l1 <- get_sig_cancer_type_index()
l2 <- get_sig_cancer_type_index(sig_type = "SBS")
l3 <- get_sig_cancer_type_index(sig_type = "DBS", source = "PCAWG", seq_type = "WGS")
l4 <- get_sig_cancer_type_index(sig_type = "ID")
l5 <- get_sig_cancer_type_index(keyword = "breast")
l1
l2
l3
l4
l5
```

get_sig_db

Get Curated Reference Signature Database

Description

Reference mutational signatures and their aetiologies, mainly obtained from COSMIC database (SigProfiler results) and cleaned before saving into `sigminer` package. You can obtain:

- COSMIC legacy SBS signatures.
- COSMIC v3 SBS signatures.
- COSMIC v3 DBS signatures.
- COSMIC v3 ID (indel) signatures.
- SBS and RS (rearrangement) signatures from Nik lab 2020 Nature Cancer paper.
- RS signatures from BRCA560 and USARC cohorts.
- Copy number signatures from USARC cohort and TCGA.

Usage

`get_sig_db(sig_db = "legacy")`

Arguments

- `sig_db` default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIC v3 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to refer reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. UPDATE, the latest version of reference version can be automatically downloaded and loaded from https://cancer.
`get_sig_db` at `sanger.ac.uk/signatures/downloads/` when an option with latest_ prefix is specified (e.g. "latest_SBS_GRCh37"). **Note:** the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

**Value**

a list.

**References**


**See Also**

`get FileInfo` and `show_cosmicSigProfile`.

**Examples**

```r
s1 <- get_sig_db()
s2 <- get_sig_db("SBS")
s3 <- get_sig_db("DBS")
s4 <- get_sig_db("DBS_mm10")
s5 <- get_sig_db("SBS_Nik_lab")
s6 <- get_sig_db("ID")
s7 <- get_sig_db("RS_BRCA560")
s8 <- get_sig_db("RS_USARC")
s9 <- get_sig_db("RS_Nik_lab")
s10 <- get_sig_db("CNS_USARC")
s11 <- get_sig_db("CNS_TCGA")
```
get_sig_exposure

Get Signature Exposure from 'Signature' Object

Description

The expected number of mutations (or copy number segment records) with each signature was determined after a scaling transformation \( V \sim WH = W'H' \) where \( W' = WU' \) and \( H' = UH \). The scaling matrix \( U \) is a \( K \times K \) diagonal matrix (\( K \) is signature number, \( U' \) is the inverse of \( U \)) with the element corresponding to the L1-norm of column vectors of \( W \) (i.e., the sum of the elements of the vector). As a result, the \( k \)-th row vector of the final matrix \( H' \) represents the absolute exposure (activity) of the \( k \)-th process across samples (e.g., for SBS, the estimated (or expected) number of mutations generated by the \( k \)-th process). Of note, for copy number signatures, only components of feature \( CN \) was used for calculating \( H' \).

Usage

```r
get_sig_exposure(
  Signature,
  type = c("absolute", "relative"),
  rel_threshold = 0.01
)
```

Arguments

- **Signature**: a Signature object obtained either from `sig_extract` or `sig_auto_extract`, or just a raw exposure matrix with column representing samples (patients) and row representing signatures.
- **type**: 'absolute' for signature exposure and 'relative' for signature relative exposure.
- **rel_threshold**: only used when type is 'relative', relative exposure less than (\( \leq \)) this value will be set to 0 and thus all signature exposures may not sum to 1. This is similar to this argument in `sig_fit`.

Value

a data.table

Author(s)

Shixiang Wang w_shixiang@163.com

References

get_sig_feature_association

Calculate Association between Signature Exposures and Other Features

Description

Association of signature exposures with other features will be performed using one of two procedures: for a continuous association variable (including ordinal variable), correlation is performed; for a binary association variable, samples will be divided into two groups and Mann-Whitney U-test is performed to test for differences in signature exposure medians between the two groups. See get_tidy_association for cleaning association result.

Usage

get_sig_feature_association(
  data,
  cols_to_sigs,
  cols_to_features,
  type = "ca",
  method_co = c("spearman", "pearson", "kendall"),
  method_ca = stats::wilcox.test,
  min_n = 0.01,
  verbose = FALSE,
  ...
)

Arguments

data a data.frame contains signature exposures and other features
cols_to_sigs colnames for signature exposure
cols_to_features colnames for other features
type a character vector containing 'ca' for categorical variable and 'co' for continuous variable, it must have the same length as cols_to_features.

Examples

# Load mutational signature
load(system.file("extdata", "toy_mutational_signature.RData",
  package = "sigminer", mustWork = TRUE))

# Get signature exposure
expo1 <- get_sig_exposure(sig2)
expo1

expo2 <- get_sig_exposure(sig2, type = "relative")
expo2
get_sig_rec_similarity

method_co  method for continuous variable, default is "spearman", could also be "pearson" and "kendall".
method_ca  method for categorical variable, default is "wilcox.test"
min_n      a minimal fraction (e.g. 0.01) or an integer number (e.g. 10) for filtering some variables with few positive events. Default is 0.01.
verbose    if TRUE, print extra message.
...        other arguments passing to test functions, like cor.test.

Value

a list. For 'co' features, 'measure' means correlation coefficient. For 'ca' features, 'measure' means difference in means of signature exposure.

See Also

get_tidy_association

get_sig_rec_similarity

Get Reconstructed Profile Cosine Similarity, RSS, etc.

Description

See bp_extract_signatures for examples.

Usage

get_sig_rec_similarity(Signature, nmf_matrix)

Arguments

Signature    a Signature object.
nmf_matrix   a matrix used for NMF decomposition with rows indicate samples and columns indicate components.

Value

a data.table.
get_sig_similarity

Calculate Similarity between Identified Signatures and Reference Signatures

Description

The reference signatures can be either a Signature object specified by Ref argument or known COSMIC signatures specified by sig_db argument. Two COSMIC databases are used for comparisons - "legacy" which includes 30 signatures, and "SBS" - which includes updated/refined 65 signatures. This function is modified from compareSignatures() in maftools package. **NOTE:** all reference signatures are generated from gold standard tool: SigProfiler.

Usage

```r
get_sig_similarity(
  Signature,
  Ref = NULL,
  sig_db = c("legacy", "SBS", "DBS", "ID", "TSB", "SBS_Nik_lab", "RS_Nik_lab", "RS_BRCA560", "RS_USARC", "CNS_USARC", "CNS_TCGA", "SBS_hg19", "SBS_hg38", "SBS_mm9", "SBS_mm10", "DBS_hg19", "DBS_hg38", "DBS_mm9", "DBS_mm10", "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "latest_SBS_GRCh37", "latest_DBS_GRCh37", "latest_ID_GRCh37", "latest_SBS_GRCh38", "latest_DBS_GRCh38", "latest_SBS_mm9", "latest_DBS_mm9", "latest_SBS_mm10", "latest_DBS_mm10", "latest_SBS_mm6", "latest_DBS_mm6"),
  db_type = c("", "human-exome", "human-genome"),
  method = "cosine",
  normalize = c("row", "feature"),
  feature_setting = sigminer::CN.features,
  set_order = TRUE,
  pattern_to_rm = NULL,
  verbose = TRUE
)
```

Arguments

- **Signature**: a Signature object or a component-by-signature matrix/data.frame (sum of each column is 1) or a normalized component-by-sample matrix/data.frame (sum of each column is 1). More please see examples.
- **Ref**: default is NULL, can be a same object as Signature.
- **sig_db**: default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40
get_sig_similarity categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. **UPDATE**, the latest version of reference version can be automatically downloaded and loaded from [https://cancer.sanger.ac.uk/signatures/downloads/](https://cancer.sanger.ac.uk/signatures/downloads/) when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). **Note**: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

db_type only used when sig_db is enabled. "" for keeping default, "human-exome" for transforming to exome frequency of component, and "human-genome" for transforming to whole genome frequency of component. Currently only works for 'SBS'.

method default is 'cosine' for cosine similarity.

normalize one of "row" and "feature". "row" is typically used for common mutational signatures. "feature" is designed by me to use when input are copy number signatures.

feature_setting a data.frame used for classification. **Only used when method is "Wang" ("W")**. Default is CN.features. Users can also set custom input with "feature", "min" and "max" columns available. Valid features can be printed by unique(CN.features$feature).

set_order if TRUE, order the return similarity matrix.

pattern_to_rm patterns for removing some features/components in similarity calculation. A vector of component name is also accepted. The remove operation will be done after normalization. Default is NULL.

verbose if TRUE, print extra info.

Value

a list containing similarities, aetiologies if available, best match and RSS.

Author(s)

Shixiang Wang w_shixiang@163.com

References


Examples

```r
# Load mutational signature
data = read.csv(system.file("extdata\toy_mutational_signature.RData", package = "sigminer", mustWork = TRUE))
s1 <- get_sig_similarity(sig2, Ref = sig2)
s1
s2 <- get_sig_similarity(sig2)
s2
s3 <- get_sig_similarity(sig2, sig_db = "SBS")
s3

# Set order for result similarity matrix
s4 <- get_sig_similarity(sig2, sig_db = "SBS", set_order = TRUE)
s4

## Remove some components
## in similarity calculation
)
s5

## Same to DBS and ID signatures
x1 <- get_sig_db("DBS_hg19")
x2 <- get_sig_db("DBS_hg38")
s6 <- get_sig_similarity(x1$db, x2$db)
s6
```

---

**get_tidy_association**

Get Tidy Signature Association Results

**Description**

Get Tidy Signature Association Results

**Usage**

```r
get_tidy_association(cor_res, p_adjust = FALSE, method = "fdr")
```
Arguments

- `cor_res` data returned by `get_sig_feature_association()`
- `p_adjust` logical, if TRUE, adjust p values by data type.
- `method` p value correction method, see `stats::p.adjust` for more detail.

Value

a data.frame

See Also

`get_sig_feature_association`

------------------------------------------------------------------------

**group_enrichment**  General Group Enrichment Analysis

------------------------------------------------------------------------

Description

This function takes a data.frame as input, compares proportion of positive cases or mean measure in one subgroup and the remaining samples.

Usage

```r
group_enrichment(
  df,
  grp_vars = NULL,
  enrich_vars = NULL,
  cross = TRUE,
  co_method = c("t.test", "wilcox.test"),
  ref_group = NA
)
```

Arguments

- `df` a data.frame.
- `grp_vars` character vector specifying group variables to split samples into subgroups (at least 2 subgroups, otherwise this variable will be skipped).
- `enrich_vars` character vector specifying measure variables to be compared. If variable is not numeric, only binary cases are accepted in the form of TRUE/FALSE or P/N (P for positive cases and N for negative cases). Of note, NA values set to negative cases.
- `cross` logical, default is TRUE, combine all situations provided by `grp_vars` and `enrich_vars`. For examples, `c('A', 'B')` and `c('C', 'D')` will construct 4 combinations (i.e. "AC", "AD", "BC" and "BD"). A variable can not be in both `grp_vars` and `enrich_vars`, such cases will be automatically drop. If FALSE, use pairwise combinations, see section "examples" for use cases.
co_method: test method for continuous variable, default is 't.test'.
ref_group: reference group set in grp_vars.

Value

a data.table with following columns:

- `grp_var`: group variable name.
- `enrich_var`: enrich variable (variable to be compared) name.
- `grp1`: the first group name, should be a member in `grp_var` column.
- `grp2`: the remaining samples, marked as 'Rest'.
- `grp1_size`: sample size for `grp1`.
- `grp1_pos_measure`: for binary variable, it stores the proportion of positive cases in `grp1`; for continuous variable, it stores mean value.
- `grp2_size`: sample size for `grp2`.
- `grp2_pos_measure`: same as `grp1_pos_measure` but for `grp2`.
- `measure_observed`: for binary variable, it stores odds ratio; for continuous variable, it stores scaled mean ratio.
- `measure_tested`: only for binary variable, it stores estimated odds ratio and its 95% CI from `fisher.test()`.
- `p_value`: for binary variable, it stores p value from `fisher.test()`; for continuous variable, it stores value from `wilcox.test()` or `t.test()`.
- `type`: one of "binary" and "continuous".
- `method`: one of "fish.test", "wilcox.test" and "t.test".

See Also

`show_group_enrichment`

Examples

```r
set.seed(1234)
df <- dplyr::tibble(
  g1 = factor(abs(round(rnorm(99, 0, 1)))),
  g2 = rep(LETTERS[1:4], c(50, 40, 8, 1)),
  e1 = sample(c("P", "N"), 99, replace = TRUE),
  e2 = rnorm(99)
)
print(str(df))
print(head(df))

# Compare g1:e1, g1:e2, g2:e1 and g2:e2
x1 <- group_enrichment(df, grp_vars = c("g1", "g2"), enrich_vars = c("e1", "e2"))
x1

# Only compare g1:e1, g2:e2
```
```r
x2 <- group_enrichment(df, 
  grp_vars = c("g1", "g2"), 
  enrich_vars = c("e1", "e2"), 
  co_method = "wilcox.test", 
  cross = FALSE 
)
x2

# Visualization
p1 <- show_group_enrichment(x1, fill_by_p_value = TRUE)
p1
p2 <- show_group_enrichment(x1, fill_by_p_value = FALSE)
p2
p3 <- show_group_enrichment(x1, return_list = TRUE)
p3
```

---

**handle_hyper_mutation**  
*Handle Hypermutant Samples*

**Description**

This can be used for SNV/INDEL count matrix. For copy number analysis, please skip it.

**Usage**

```r
handle_hyper_mutation(nmf_matrix)
```

**Arguments**

- `nmf_matrix`  
a matrix used for NMF decomposition with rows indicate samples and columns indicate components.

**Value**

- a matrix.

**References**

**Description**

Say Hello to Users

**Usage**

```r
hello()
```

**Examples**

```r
hello()
```

---

**MAF-class**

**Class MAF**

**Description**

S4 class for storing summarized MAF. It is from `maftools` package.

**Details**

More about MAF object please see `maftools`.

**Slots**

- `data`: data.table of MAF file containing all non-synonymous variants.
- `variants.per.sample`: table containing variants per sample
- `variant.type.summary`: table containing variant types per sample
- `variant.classification.summary`: table containing variant classification per sample
- `gene.summary`: table containing variant classification per gene
- `summary`: table with basic MAF summary stats
- `maf.silent`: subset of main MAF containing only silent variants
- `clinical.data`: clinical data associated with each sample/Tumor_Sample_Barcode in MAF.
Description

Output Signature Bootstrap Fitting Results

Usage

```
output_bootstrap(x, result_dir, mut_type = "SBS", sig_db = mut_type)
```

Arguments

- `x` result from `sig_fit_bootstrap_batch`.
- `result_dir` a result directory.
- `mut_type` one of 'SBS', 'DBS', 'ID' or 'CN'.
- `sig_db` default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. UPDATE, the latest version of reference version can be automatically downloaded and loaded from `https://cancer.sanger.ac.uk/signatures/downloads/` when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). Note: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

Value

Nothing.
output_fit

Output Signature Fitting Results

Description

Output Signature Fitting Results

Usage

output_fit(x, result_dir, mut_type = "SBS", sig_db = mut_type)

Arguments

x : result from sig_fit.
result_dir : a result directory.
mut_type : one of 'SBS', 'DBS', 'ID' or 'CN'.
sig_db : default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to refer reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. UPDATE, the latest version of reference version can be automatically downloaded and loaded from https://cancer.sanger.ac.uk/signatures/downloads/ when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). 

Note: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

Value

Nothing.
output_sig

Output Signature Results

Description

Output Signature Results

Usage

```
output_sig(sig, result_dir, mut_type = "SBS", sig_db = mut_type)
```

Arguments

- `sig`  
a Signature object.
- `result_dir`  
a result directory.
- `mut_type`  
one of 'SBS', 'DBS', 'ID' or 'CN'.
- `sig_db`  
default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. **UPDATE**, the latest version of reference version can be automatically downloaded and loaded from https://cancer.sanger.ac.uk/signatures/downloads/ when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). **Note:** the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

Value

Nothing.
**output_tally**  
*Output Tally Result in Barplots*

**Description**
Output Tally Result in Barplots

**Usage**
```
output_tally(x, result_dir, mut_type = "SBS")
```

**Arguments**
- `x`: a matrix with row representing components (motifs) and column representing samples.
- `result_dir`: a result directory.
- `mut_type`: one of 'SBS', 'DBS', 'ID' or 'CN'.

**Value**
Nothing.

**read_copynumber**  
*Read Absolute Copy Number Profile*

**Description**
Read absolute copy number profile for preparing CNV signature analysis. See detail part of `sig_tally()` to see how to handle sex to get correct summary.

**Usage**
```
read_copynumber(
  input,
  pattern = NULL,
  ignore_case = FALSE,
  seg_cols = c("Chromosome", "Start.bp", "End.bp", "modal_cn"),
  samp_col = "sample",
  add_loh = FALSE,
  loh_min_len = 10000,
  loh_min_frac = 0.05,
  join_adj_seg = TRUE,
  skip_annotation = FALSE,
  use_all = add_loh,
  min_segnum = 0L,
```
max_copynumber = 20L,
genome_build = c("hg19", "hg38", "mm10", "mm9"),
genome_measure = c("called", "wg"),
complement = FALSE,
...)

Arguments

input a data.frame or a file or a directory contains copy number profile.
pattern an optional regular expression used to select part of files if input is a directory, more detail please see list.files() function.
ignore_case logical. Should pattern-matching be case-insensitive?
seg_cols four strings used to specify chromosome, start position, end position and copy number value in input, respectively. Default use names from ABSOLUTE calling result.
samp_col a character used to specify the sample column name. If input is a directory and cannot find samp_col, sample names will use file names (set this parameter to NULL is recommended in this case).
add_loh if TRUE, add LOH labels to segments. **NOTE** a column 'minor_cn' must exist to indicate minor allele copy number value. Sex chromosome will not be labeled.
loh_min_len The length cut-off for labeling a segment as 'LOH'. Default is 10Kb.
loh_min_frac When join_adj_seg set to TRUE, only the length fraction of LOH region is larger than this value will be labeled as 'LOH'. Default is 30%.
join_adj_seg if TRUE (default), join adjacent segments with same copy number value. This is helpful for precisely count the number of breakpoint. When set use_all=TRUE, the mean function will be applied to extra numeric columns and unique string columns will be pasted by comma for joined records.
skip_annotation if TRUE, skip annotation step, it may affect some analysis and visualization functionality, but speed up reading data.
use_all default is FALSE. If True, use all columns from raw input.
min_segnum minimal number of copy number segments within a sample.
max_copynumber bigger copy number within a sample will be reset to this value.
genome_build genome build version, should be 'hg19', 'hg38', 'mm9' or 'mm10'.
genome_measure default is 'called', can be 'wg' or 'called'. Set 'called' will use called segments size to compute total size for CNA burden calculation, this option is useful for WES and target sequencing. Set 'wg' will use autosome size from genome build, this option is useful for WGS, SNP etc..
complement if TRUE, complement chromosome (except 'Y') does not show in input data with normal copy 2.
... other parameters pass to data.table::fread()
read_copynumber_ascat

Value

A CopyNumber object.

Author(s)

Shixiang Wang w_shixiang@163.com

See Also

read_maf for reading mutation data to MAF object.

Examples

```r
# Load toy dataset of absolute copynumber profile
load(system.file("extdata", "toy_segTab.RData",
               package = "sigminer", mustWork = TRUE ))

## read_copynumber

## subset

cn_subset <- subset(cn, sample == "TCGA-DF-A2KN-01A-11D-A17U-01")

# Add LOH

set.seed(1234)
segs$minor_cn <- sample(c(0, 1), size = nrow(segs), replace = TRUE)

## read_copynumber

cn <- read_copynumber(segs,
                       seg_cols = c("chromosome", "start", "end", "segVal"),
                       genome_build = "hg19", complement = FALSE)

# Use tally method "S" (Steele et al.)

tally_s <- sig_tally(cn, method = "S")

## read_copynumber

tab_file <- system.file("extdata", "metastatic_tumor.segtab.txt",
                        package = "sigminer", mustWork = TRUE )

## read_copynumber

cn2 <- read_copynumber(tab_file)

## read_copynumber
```

---

**Description**

Note, the result is not a CopyNumber object, you need to generate it by yourself.

**Usage**

```r
read_copynumber_ascat(x)
```

---

**Description**

Read Copy Number Data from ASCAT Result Files

**Usage**

```r
read_copynumber_ascat(x)
```
read_copynumber_seqz

Arguments

- `x` one or more .rds format files which contains ASCAT object from result of ascat.runAscat() in ASCAT package.

Value

- a tidy list.

Description

Read Absolute Copy Number Profile from Sequenza Result Directory

Usage

read_copynumber_seqz(target_dir, return_df = FALSE, ...)

Arguments

- `target_dir` a directory path.
- `return_df` if TRUE, return a data.frame directly, otherwise return a CopyNumber object.
- `...` other parameters passing to read_copynumber().

Value

- a data.frame or a CopyNumber object.

read_maf

Read MAF Files

Description

This function is a wrapper of maftools::read.maf. Useless options in maftools::read.maf are dropped here. You can also use maftools::read.maf to read the data. All reference alleles and mutation alleles should be recorded in positive strand format.

Usage

read_maf(maf, verbose = TRUE)
Arguments

- **maf**
  - Tab delimited MAF file. File can also be gz compressed. Required. Alternatively, you can also provide already read MAF file as a dataframe.
- **verbose**
  - TRUE logical. Default to be talkative and prints summary.

See Also

- `read_copynumber` for reading copy number data to CopyNumber object.

Examples

```r
laml.maf <- system.file("extdata", "tcga_laml.maf.gz", package = "maftools", mustWork = TRUE)
if (!require("R.utils")) {
  message("Please install 'R.utils' package firstly")
} else {
  laml <- read_maf(maf = laml.maf)
  laml
}
```

---

**read_sv_as_rs**  
*Read Structural Variation Data as RS object*

Description

Read Structural Variation Data as RS object

Usage

```r
read_sv_as_rs(input)
```

Arguments

- **input**
  - A data.frame or a file with the following columns: "sample", "chr1", "start1", "end1", "chr2", "start2", "end2", "strand1", "strand2", "svclass". NOTE: If column "svclass" already exists in input, "strand1" and "strand2" are optional. If "svclass" is not provided, `read_sv_as_rs()` will compute it by "strand1","strand2"(strand1/strand2),"chr1" and "chr2":
  - translocation, if mates are on different chromosomes.
  - inversion (+/-) and (-/+), if mates on the same chromosome.
  - deletion (+/+), if mates on the same chromosome.
  - tandem-duplication (-/-), if mates on the same chromosome.

Value

A list
read_vcf

Examples

sv <- readRDS(system.file("extdata", "toy_sv.rds", package = "sigminer", mustWork = TRUE))
rs <- read_sv_as_rs(sv)
# svclass is optional
rs2 <- read_sv_as_rs(sv[, setdiff(colnames(sv), "svclass")])
identical(rs, rs2)
tally_rs <- sig_tally(rs)

---

### read_vcf

**Read VCF Files as MAF Object**

**Description**

MAF file is more recommended. In this function, we will mimic the MAF object from the key c(1, 2, 4, 5, 7) columns of VCF file.

**Usage**

```r
read_vcf(
  vcfs,
  samples = NULL,
  genome_build = c("hg19", "hg38", "mm10", "mm9"),
  keep_only_pass = FALSE,
  verbose = TRUE
)
```

**Arguments**

- **vcfs** VCF file paths.
- **samples** sample names for VCF files.
- **genome_build** genome build version like "hg19".
- **keep_only_pass** if TRUE, keep only 'PASS' mutation for analysis.
- **verbose** if TRUE, print extra info.

**Value**

a MAF.

**See Also**

read_maf, read_copynumber
read_xena_variants

Examples

vcfs <- list.files(system.file("extdata", package = "sigminer"), "*.vcf", full.names = TRUE)
maf <- read_vcf(vcfs)
maf <- read_vcf(vcfs, keep_only_pass = TRUE)

---

read_xena_variants  Read UCSC Xena Variant Format Data as MAF Object

Description

Read UCSC Xena Variant Format Data as MAF Object

Usage

read_xena_variants(path)

Arguments

path  a path to variant file.

Value

a MAF object.

Examples

if (requireNamespace("UCSCXenaTools")) {
  library(UCSCXenaTools)
  options(use_hiplot = TRUE)
  example_file <- XenaGenerate(subset = XenaDatasets == "mc3/ACC_mc3.txt") %>%
    XenaQuery() %>%
    XenaDownload()
  x <- read_xena_variants(example_file$destfiles)
x@data
  y <- sig_tally(x)
y
}
**report_bootstrap_p_value**

*Report P Values from bootstrap Results*

**Description**

See examples in `sig_fit_bootstrap`.

**Usage**

```r
report_bootstrap_p_value(x, thresholds = c(0.01, 0.05, 0.1))
```

**Arguments**

- `x` a (list of) result from `sig_fit_bootstrap`.
- `thresholds` a vector of relative exposure threshold for calculating p values.

**Value**

a (list of) matrix

---

**same_size_clustering** *Same Size Clustering*

**Description**

This is a wrapper for several implementation that classify samples into same size clusters, the details please see this blog. The source code is modified based on code from the blog.

**Usage**

```r
same_size_clustering(
  mat,
  diss = FALSE,
  cls = NULL,
  algo = c("nnit", "hcbottom", "kmvar"),
  method = c("maxd", "random", "mind", "elki", "ward.D", "average", "complete", "single")
)
```

**Arguments**

- `mat` a data/distance matrix.
- `diss` if TRUE, treat mat as a distance matrix.
- `cls` integer, number of sample within a cluster.
- `algo` algorithm.
- `method` method.
Value

- a vector.

Examples

```r
set.seed(1234L)
x <- rbind(
  matrix(rnorm(100, sd = 0.3), ncol = 2),
  matrix(rnorm(100, mean = 1, sd = 0.3), ncol = 2)
)
colnames(x) <- c("x", "y")
y1 <- same_size_clustering(x, clsize = 10)
y11 <- same_size_clustering(as.matrix(dist(x)), clsize = 10, diss = TRUE)
y2 <- same_size_clustering(x, clsize = 10, algo = "hcbottom", method = "ward.D")
y3 <- same_size_clustering(x, clsize = 10, algo = "kmvar")
y33 <- same_size_clustering(as.matrix(dist(x)), clsize = 10, algo = "kmvar", diss = TRUE)
```

scoring

### Description

Returns quantification of copy number profile and events including tandem duplication and Chromothripsis etc. Only copy number data from autosome is used here. **Some of the quantification methods are rough, you use at your risk.** You should do some extra work to check the result scores.

#### Usage

```r
scoring(object, TD_size_cutoff = c(1000, 1e+05, 2e+06), TD_cn_cutoff = Inf)
```

#### Arguments

- **object**: a object of CopyNumber.
- **TD_size_cutoff**: a length-3 numeric vector used to specify the start, midpoint, end segment size for determining tandem duplication size range, midpoint is used to split TD into short TD and long TD. Default is 1Kb to 100Kb for short TD, 100Kb to 2Mb for long TD.
- **TD_cn_cutoff**: a number defining the maximum copy number of TD, default is Inf, i.e. no cutoff.
Value

a data.table with following scores:

- cnaBurden: CNA burden representing the altered genomic fraction as previously reported.
- cnaLoad: CNA load representing the quantity of copy number alteration.
- MACN: mean altered copy number (MACN) reflecting the property of altered copy number segments, calculated as
  \[ MACN = \frac{\sum_i CN_i}{N_{cnv}} \]
  where \( CN_i \) is the copy number of altered segment \( i \), \( N_{cnv} \) is the number of CNV.
- weightedMACN: same as MACN but weighted with segment length.
  \[ MACN_{weighted} = \frac{\sum_i (CN_i \times L_i)}{\sum_i L_i} \]
  where \( L_i \) is the length of altered copy number segment \( i \).
- Ploidy: ploidy, the formula is same as weightedMACN but using all copy number segments instead of altered copy number segments.
- TDP_pnas: tandem duplication phenotype score from https://www.pnas.org/doi/10.1073/pnas.1520010113, the threshold \( k \) in reference is omitted.
  \[ TDP = \frac{-\sum_{chr} |TD_{obs} - TD_{exp}|}{TD_{total}} \]
  where \( TD_{total} \) is the number of TD, \( TD_{obs} \) and \( TD_{exp} \) are observed number of TD and expected number of TD for each chromosome.
- TDP: tandem duplication score used defined by our group work, TD represents segment with copy number greater than 2.
  \[ TD = \frac{TD_{total}}{\sum_{chr} |TD_{obs} - TD_{exp}| + 1} \]
- sTDP: TDP score for short TD.
- lTDP: TDP score for long TD.
- TDP_size : TDP region size (Mb).
- sTDP_size: sTDP region size (Mb).
- lTDP_size: lTDP region size(Mb).
- Chromoth_state: chromothripsis state score, according to reference doi:10.1016/j.cell.2013.02.023, chromothripsis frequently leads to massive loss of segments on the affected chromosome with segmental losses being interspersed with regions displaying normal (disomic) copy-number (e.g., copy-number states oscillating between copy-number = 1 and copy-number = 2), form tens to hundreds of locally clustered DNA rearrangements. Most of methods use both SV and CNV to infer chromothripsis, here we roughly quantify it with
  \[ \sum_{chr} N_{oscCN}^2 \]
  where \( N_{oscCN} \) is the number of oscillating copy number pattern "2-1-2" for each chromosome.
show_catalogue

**Examples**

```r
# Load copy number object
load(system.file("extdata", "toy_copynumber.RData",
    package = "sigminer", mustWork = TRUE))

d <- scoring(cn)
d

d2 <- scoring(cn, TD_cn_cutoff = 4L)
d2
```

---

**show_catalogue**

*Show Alteration Catalogue Profile*

**Description**

Show Alteration Catalogue Profile

**Usage**

```r
show_catalogue(
    catalogue,
    mode = c("SBS", "copynumber", "DBS", "ID", "RS"),
    method = "Wang",
    normalize = c("raw", "row", "feature"),
    style = c("default", "cosmic"),
    samples = NULL,
    samples_name = NULL,
    x_lab = "Components",
    y_lab = "Counts",
    ...
)
```

**Arguments**

- **catalogue**: result from `sig_tally` or a matrix with row representing components (motifs) and column representing samples.
- **mode**: signature type for plotting, now supports 'copynumber', 'SBS', 'DBS', 'ID' and 'RS' (genome rearrangement signature).
- **method**: method for copy number feature classification in `sig_tally`, can be one of "Wang" ("W"), "S".
- **normalize**: normalize method.
- **style**: plot style, one of 'default' and 'cosmic'.
- **samples**: default is NULL, show sum of all samples in one row. If not NULL, show specified samples.
show_cn_circos

samples_name set the sample names shown in plot.

x_lab x axis lab.

y_lab y axis lab.

... other arguments passing to show_sig_profile.

Value

a ggplot object

Examples

data(“simulated_catalogs”) p <- show_catalogue(simulated_catalogs$set1, style = “cosmic”) p

Description

Another visualization method for copy number profile like show_cn_profile.

Usage

show_cn_circos(
  data,
  samples = NULL,
  show_title = TRUE,
  chrs = paste0(“chr”, 1:22),
  genome_build = c(“hg19”, “hg38”, “mm10”, “mm9”),
  col = NULL,
  side = “inside”,
  ...
)

Arguments

data a CopyNumber object or a data.frame containing at least ‘chromosome’, ‘start’, ‘end’, ‘segVal’ these columns.
samples default is NULL, can be a character vector representing multiple samples or number of samples to show. If data argument is a data.frame, a column called sample must exist.
show_title if TRUE (default), show title with sample ID.
chrs chromosomes start with ‘chr’.
genome_build genome build version, used when data is a data.frame, should be ’hg19’ or ’hg38’.
show_cn_components

Show Copy Number Components

Description
Show classified components ("Wang" ("W") method) for copy number data.

Usage

```
show_cn_components(
    parameters,
    method = "Wang",
    show_weights = TRUE,
    log_y = FALSE,
    return_plotlist = FALSE,
    base_size = 12,
    nrow = 2,
```

Value
a circos plot
show_cn_distribution

    align = "hv",
    ...
)

Arguments

parameters     a data.frame contain parameter components, obtain this from sig_tally function.
method         method for feature classification, can be one of "Wang" ("W"), "S" (for method described in Steele et al. 2019).
show_weights   default is TRUE, show weights for each component. Only used when method is "Macintyre".
log_y          logical, if TRUE, show log10 based y axis, only works for input from "Wang" ("W") method.
return_plotlist if TRUE, return a list of ggplot objects but a combined plot.
base_size      overall font size.
nrow            (optional) Number of rows in the plot grid.
align           (optional) Specifies whether graphs in the grid should be horizontally ("h") or vertically ("v") aligned. Options are "none" (default), "hv" (align in both directions), "h", and "v".
...

other options pass to plot_grid function of cowplot package.

Value

a ggplot object

Author(s)

Shixiang Wang w_shixiang@163.com

show_cn_distribution  Show Copy Number Distribution either by Length or Chromosome

Description

Visually summarize copy number distribution either by copy number segment length or chromosome. Input is a CopyNumber object, genome_build option will read from genome_build slot of object.
show_cn_distribution

Usage

```r
show_cn_distribution(
  data,
  rm_normal = TRUE,
  mode = c("ld", "cd"),
  fill = FALSE,
  scale_chr = TRUE,
  base_size = 14
)
```

Arguments

data
  a CopyNumber object.

rm_normal
  logical. Whether remove normal copy (i.e. "segVal" equals 2), default is TRUE.

mode
  either "ld" for distribution by CN length or "cd" for distribution by chromosome.

fill
  when mode is "cd" and fill is TRUE, plot percentage instead of count.

scale_chr
  logical. If TRUE, normalize count to per Megabase unit.

base_size
  overall font size.

Value

a ggplot object

Author(s)

Shixiang Wang w_shixiang@163.com

Examples

```r
# Load copy number object
load(system.file("extdata", "toy_copynumber.RData",
               package = "sigminer", mustWork = TRUE))
# Plot distribution
p1 <- show_cn_distribution(cn)
p1
p2 <- show_cn_distribution(cn, mode = "cd")
p2
p3 <- show_cn_distribution(cn, mode = "cd", fill = TRUE)
p3
```
show_cn_features  

Description

Show Copy Number Feature Distributions

Usage

show_cn_features(
  features,
  method = "Wang",
  rm_outlier = FALSE,
  ylab = NULL,
  log_y = FALSE,
  return_plotlist = FALSE,
  base_size = 12,
  nrow = 2,
  align = "hv",
  ...
)

Arguments

- **features**: a feature list generate from `sig_tally` function.
- **method**: method for feature classification, can be one of "Wang" ("W"), "S" (for method described in Steele et al. 2019).
- **rm_outlier**: default is FALSE, if TRUE, remove outliers. Only works when method is "Wang" ("W").
- **ylab**: lab of y axis.
- **log_y**: logical, if TRUE, show log10 based y axis, only works for input from "Wang" ("W") method.
- **return_plotlist**: if TRUE, return a list of ggplot objects but a combined plot.
- **base_size**: overall font size.
- **nrow**: (optional) Number of rows in the plot grid.
- **align**: (optional) Specifies whether graphs in the grid should be horizontally ("h") or vertically ("v") aligned. Options are "none" (default), "hv" (align in both directions), "h", and "v".
- **...**: other options pass to `plot_grid` function of cowplot package.

Value

- a ggplot object
show_cn_freq_circos  

Show Copy Number Variation Frequency Profile with Circos

Description
Show Copy Number Variation Frequency Profile with Circos

Usage

```
show_cn_freq_circos(
  data,
  groups = NULL,
  cutoff = 2L,
  resolution_factor = 1L,
  title = c("AMP", "DEL"),
  chrs = paste0("chr", 1:22),
  genome_build = c("hg19", "hg38", "mm10", "mm9"),
  cols = NULL,
  plot_ideogram = TRUE,
  track_height = 0.5,
  ideogram_height = 1,
  ...
)
```

Arguments

data  
a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal', 'sample' these columns.
groups  
a named list or a column name for specifying groups.
cutoff  
copy number value cutoff for splitting data into AMP and DEL. The values equal to cutoff are discarded. Default is 2, you can also set a length-2 vector, e.g. c(2, 2).
resolution_factor  
an integer to control the resolution. When it is 1 (default), compute frequency in each cytoband. When it is 2, use compute frequency in each half cytoband.
title  
length-2 titles for AMP and DEL.
chrs  
chromosomes start with 'chr'.
genome_build  
genome build version, used when data is a data.frame, should be 'hg19' or 'hg38'.
cols  
length-2 colors for AMP and DEL.
plot_ideogram  
default is TRUE, show ideogram.
track_height  
track height in mm unit.
ideogram_height  
ideogram height in mm unit.
...  
other parameters passing to circlize::circos.genomicLines.
show_cn_group_profile

Value

Nothing.

Examples

```r
load(system.file("extdata", "toy_copynumber.RData", 
                 package = "sigminer", mustWork = TRUE 
                ))

show_cn_freq_circos(cn)
ss <- unique(cn@data$sample)
show_cn_freq_circos(cn, groups = list(a = ss[1:5], b = ss[6:10]), cols = c("red", "green"))
```

Description

Show Summary Copy Number Profile for Sample Groups

Usage

```r
show_cn_group_profile(
  data, 
  groups = NULL, 
  fill_area = TRUE, 
  cols = NULL, 
  chrs = paste0("chr", c(1:22, "X")), 
  genome_build = c("hg19", "hg38", "mm10", "mm9"), 
  cutoff = 2L, 
  resolution_factor = 1L, 
  force_y_limit = TRUE, 
  highlight_genes = NULL, 
  repel = FALSE, 
  nrow = NULL, 
  ncol = NULL, 
  return_plotlist = FALSE
)
```

Arguments

- **data**: a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal', 'sample' these columns.
- **groups**: a named list or a column name for specifying groups.
- **fill_area**: default is TRUE, fill area with colors.
cols length-2 colors for AMP and DEL.
chrs chromosomes start with 'chr'.
genome_build genome build version, used when data is a data.frame, should be 'hg19' or 'hg38'.
cutoff copy number value cutoff for splitting data into AMP and DEL. The values equal to cutoff are discarded. Default is 2, you can also set a length-2 vector, e.g. c(2, 2).
resolution_factor an integer to control the resolution. When it is 1 (default), compute frequency in each cytoband. When it is 2, use compute frequency in each half cytoband.
force_y_limit default is TRUE, force multiple plots
highlight_genes gene list to highlight. have same y ranges. You can also set a length-2 numeric value.
repep if TRUE (default is FALSE), repel highlight genes to avoid overlap.
nrow number of rows in the plot grid when multiple samples are selected.
ncol number of columns in the plot grid when multiple samples are selected.
return_plotlist default is FALSE, if TRUE, return a plot list instead of a combined plot.

Value

a (list of) ggplot object.

Examples

load(system.file("extdata", "toy_copynumber.RData",
    package = "sigminer", mustWork = TRUE
))

p1 <- show_cn_group_profile(cn)
p1

ss <- unique(cn@data$sample)
p2 <- show_cn_group_profile(cn, groups = list(a = ss[1:5], b = ss[6:10]))
p2

p3 <- show_cn_group_profile(cn,
    groups = list(g1 = ss[1:5], g2 = ss[6:10]),
    force_y_limit = c(-1, 1), nrow = 2
)
p3

## Set custom cutoff for custom data
data <- cn@data
data$segVal <- data$segVal - 2L

p4 <- show_cn_group_profile(data,
    groups = list(g1 = ss[1:5], g2 = ss[6:10]),
    force_y_limit = c(-1, 1), nrow = 2,
cutoff = c(0, 0)

p4

## Add highlight gene
p5 <- show_cn_group_profile(cn, highlight_genes = c("TP53", "EGFR"))

show_cn_profile

Show Sample Copy Number Profile

Description

Sometimes it is very useful to check details about copy number profile for one or multiple samples. This function is designed to do this job and can be further modified by ggplot2 related packages.

Usage

show_cn_profile(
  data,
  samples = NULL,
  show_n = NULL,
  show_title = FALSE,
  show_labels = NULL,
  chrs = paste0("chr", 1:22),
  position = NULL,
  genome_build = c("hg19", "hg38", "mm10", "mm9"),
  ylim = NULL,
  nrow = NULL,
  ncol = NULL,
  return_plotlist = FALSE
)

Arguments

data     a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal' these columns.
samples  default is NULL, can be a character vector representing multiple samples. If data argument is a data.frame, a column called sample must exist.
show_n   number of samples to show, this is used for checking.
show_title if TRUE, show title for multiple samples.
show_labels one of NULL, "s" (for labelling short segments < 1e7) or "a" (all segments).
chrs      chromosomes start with 'chr'.
position  a position range, e.g. "chr1:3218923-116319008". Only data overlaps with this range will be shown.
show_cor

Description

All variables must be continuous. The matrix will be returned as an element of ggplot object. This is basically a wrapper of R package ggcorrplot.

Usage

show_cor(
  data,
  x_vars = colnames(data),
  y_vars = x_vars,
  cor_method = "spearman",
  vis_method = "square",
  lab = TRUE,
  test = TRUE,
  return_plotlist = FALSE,
  genome_build = genome build version, used when data is a data.frame, should be 'hg19' or 'hg38'.
  ylim = limits for y axis.
  nrow = number of rows in the plot grid when multiple samples are selected.
  ncol = number of columns in the plot grid when multiple samples are selected.
  return_plotlist = default is FALSE, if TRUE, return a plot list instead of a combined plot.
)

Examples

# Load copy number object
load(system.file("extdata", "toy_copynumber.RData",
    package = "sigminer", mustWork = TRUE
))

p <- show_cn_profile(cn, nrow = 2, ncol = 1)
p

p2 <- show_cn_profile(cn,
    nrow = 2, ncol = 1,
    position = "chr1:3218923-116319008"
)
p2

show_cor A Simple and General Way for Association Analysis
show_cor

    hc_order = FALSE,
    p_adj = NULL,
    ...
)

Arguments

data a data.frame.
x_vars variables/column names shown in x axis.
y_vars variables/column names shown in y axis.
cor_method method for correlation, default is 'spearman'.
vis_method visualization method, default is 'square', can also be 'circle'.
lab logical value. If TRUE, add correlation coefficient on the plot.
test if TRUE, run test for correlation and mark significance.
hc_order logical value. If TRUE, correlation matrix will be hc.ordered using hclust function.
p_adj p adjust method, see stats::p.adjust for details.
... other parameters passing to ggcorrplot::ggcorrplot().

Value

    a ggplot object

See Also

    show_sig_feature_corsplot for specific and more powerful association analysis and visualization.

Examples

data("mtcars")
p1 <- show_cor(mtcars)
p2 <- show_cor(mtcars,
              x_vars = colnames(mtcars)[1:4],
              y_vars = colnames(mtcars)[5:8]
)
p3 <- show_cor(mtcars, vis_method = "circle", p_adj = "fdr")
p1
p1$cor
p2
p3

    ## Auto detect problem variables
    mtcars$xx <- 0L
p4 <- show_cor(mtcars)
p4
show_cosmic  

*Show Signature Information in Web Browser*

**Description**

Show Signature Information in Web Browser

**Usage**

```
show_cosmic(x = "home")
```

**Arguments**

- `x`  
  a string indicating location ("home" for COSMIC signature home, "legacy" for COSMIC v2 signatures, "SBS" for COSMIC v3 SBS signatures, "DBS" for COSMIC v3 DBS signatures, "ID" for COSMIC v3 INDEL signatures) or signature index (e.g. "SBS1", "DBS2", "ID3").

**Value**

Nothing.

**Examples**

```r
## Not run:
show_cosmic()
show_cosmic("legacy")
show_cosmic("SBS")
show_cosmic("DBS")
show_cosmic("ID")
show_cosmic("SBS1")
show_cosmic("DBS2")
show_cosmic("ID3")
## End(Not run)
```

show_cosmic_sig_profile

*Plot Reference (Mainly COSMIC) Signature Profile*

**Description**

Plot Reference (Mainly COSMIC) Signature Profile
Usage

```r
show_cosmic_sig_profile(
  sig_index = NULL,
  show_index = TRUE,
  sig_db = "legacy",
  ...
)
```

Arguments

- `sig_index`: a vector for signature index. "ALL" for all signatures.
- `show_index`: if `TRUE`, show valid indices.
- `sig_db`: default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to refer reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. UPDATE, the latest version of reference version can be automatically downloaded and loaded from https://cancer.sanger.ac.uk/signatures/downloads/ when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). Note: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.
- `...`: other arguments passing to `show_sig_profile`.

Value

- `a ggplot object`

Author(s)

Shixiang Wang w_shixiang@163.com

Examples

```r
show_cosmic_sig_profile()
show_cosmic_sig_profile(sig_db = "SBS")
show_cosmic_sig_profile(sig_index = 1:5)
show_cosmic_sig_profile(sig_db = "SBS", sig_index = c("10a", "17a"))

gg <- show_cosmic_sig_profile(sig_index = 1:5)
gg$aetiology
```
show_groups

Show Signature Contribution in Clusters

Description
See example section in `sig_fit()` for an examples.

Usage
```
show_groups(grp_dt, ...)
```

Arguments
- `grp_dt`: a result data.table from `get_groups`.
- `...`: parameters passing to `legend()`, e.g. `x = "topleft"`.

Value
nothing.

See Also
- `get_groups`, `sig_fit`.

show_group_comparison

Plot Group Comparison Result

Description
Using result data from `get_group_comparison`, this function plots genotypes/phenotypes comparison between signature groups using `ggplot2` package and return a list of `ggplot` object contains individual and combined plots. The combined plot is easily saved to local using `cowplot::save_plot()`. Of note, default fisher test p values are shown for categorical data and fdr values are shown for continuous data.

Usage
```
show_group_comparison(
  group_comparison,
  xlab = "group",
  ylab_co = NA,
  legend_title_ca = NA,
  legend_position_ca = "bottom",
  set_ca_sig_yaxis = FALSE,
  set_ca_custom_xlab = FALSE,
```

show_group_comparison

    show_pvalue = TRUE,
    ca_p_threshold = 0.01,
    method = "wilcox.test",
    p.adjust.method = "fdr",
    base_size = 12,
    font_size_x = 12,
    text_angle_x = 30,
    text_hjust_x = 0.2,
    ...
  }
)

Arguments

  group_comparison
    a list from result of get_group_comparison function.

  xlab
    lab name of x axis for all plots. if it is NA, remove title for x axis.

  ylab_co
    lab name of y axis for plots of continuous type data. Of note, this argument
    should be a character vector has same length as group_comparison, the location
    for categorical type data should mark with NA.

  legend_title_ca
    legend title for plots of categorical type data.

  legend_position_ca
    legend position for plots of categorical type data. Of note, this argument should
    be a character vector has same length as group_comparison, the location for
    continuous type data should mark with NA.

  set_ca_sig_yaxis
    if TRUE, use y axis to show signature proportion instead of variable proportion.

  set_ca_custom_xlab
    only works when set_ca_sig_yaxis is TRUE. If TRUE, set x labels using input
    xlab, otherwise variable names will be used.

  show_pvalue
    if TRUE, show p values.

  ca_p_threshold
    a p threshold for categorical variables, default is 0.01. A p value less than 0.01
    will be shown as P < 0.01.

  method
    a character string indicating which method to be used for comparing means. It
    can be 't.test', 'wilcox.test' etc..

  p.adjust.method
    correction method, default is 'fdr'. Run p.adjust.methods to see all available
    options.

  base_size
    overall font size.

  font_size_x
    font size for x.

  text_angle_x
    text angle for x.

  text_hjust_x
    adjust x axis text

  ...

  other parameters pass to ggpubr::compare_means() or ggpubr::stat_compare_means()
  according to the specified method.
show_group_distribution

Show Groupped Variable Distribution

Value

A list of ggplot objects.

Author(s)

Shixiang Wang w_shixiang@163.com

Examples

```r
load(system.file("extdata", "toy_copynumber_signature_by_W.RData", package = "sigminer", mustWork = TRUE))

# Assign samples to clusters
groups <- get_groups(sig, method = "k-means")

set.seed(1234)

groups$prob <- rnorm(10)
groups$new_group <- sample(c("1", "2", "3", "4", NA), size = nrow(groups), replace = TRUE)

# Compare groups (filter NAs for categorical columns)
groups.cmp <- get_group_comparison(groups[, -1], col_group = "group", cols_to_compare = c("prob", "new_group"), type = c("co", "ca"), verbose = TRUE)

# Compare groups (Set NAs of categorical columns to 'Rest')
groups.cmp2 <- get_group_comparison(groups[, -1], col_group = "group", cols_to_compare = c("prob", "new_group"), type = c("co", "ca"), NAs = "Rest", verbose = TRUE)

show_group_comparison(groups.cmp)

ggcomp <- show_group_comparison(groups.cmp2)
ggcomp$co_comb
ggcomp$ca_comb
```

Description

This is a general function, it can be used in any proper analysis.
show_group_distribution

Usage

show_group_distribution(
  data,
  gvar,
  dvar,
  fun = stats::median,
  order_by_fun = FALSE,
  alpha = 0.8,
  g_label = "label",
  g_angle = 0,
  g_position = "top",
  point_size = 1L,
  segment_size = 1L,
  segment_color = "red",
  xlab = NULL,
  ylab = NULL,
  nrow = 1L,
  background_color = c("#DCDCDC", "#F5F5F5")
)

Arguments

data a data.frame.
gvar a group variable name/index.
dvar a distribution variable name/index.
fun a function to summarize, default is stats::median, can also be mean.
order_by_fun if TRUE, reorder the groups by summary measure computed by argument fun.
alpha alpha for points, range from 0 to 1.
g_label a string 'label' (default) for labeling with sample size, or 'norm' to show just group name, or a named vector to set facet labels.
g_angle angle for facet labels, default is 0.
g_position position for facet labels, default is 'top', can also be 'bottom'.
point_size size of point.
segment_size size of segment.
segment_color color of segment.
xlab title for x axis.
ylab title for y axis.
nrow number of row.
background_color background color for plot panel.

Value

a ggplot object.
show_group_enrichment

Author(s)
Shixiang Wang w_shixiang@163.com

Examples
set.seed(1234)
data <- data.frame(
  yval = rnorm(120),
  gr = c(rep("A", 50), rep("B", 40), rep("C", 30))
)
p <- show_group_distribution(data,
gvar = 2, dvar = 1,
g_label = "norm",
background_color = "grey"
)
p
p2 <- show_group_distribution(data,
gvar = "gr", dvar = "yval",
g_position = "bottom",
order_by_fun = TRUE,
alpha = 0.3
)
p2

# Set custom group names
p3 <- show_group_distribution(data,
gvar = 2, dvar = 1,
g_label = c("A" = "X", "B" = "Y", "C" = "Z")
)
p3

show_group_enrichment  Show Group Enrichment Result

Description
See group_enrichment for examples. NOTE the box fill and the box text have different meanings.

Usage
show_group_enrichment(
df_enrich,
return_list = FALSE,
scales = "free",
add_text_annotation = TRUE,
fill_by_p_value = TRUE,
use_fdr = TRUE,
cut_p_value = FALSE,
cut_breaks = c(-Inf, -5, log10(0.05), -log10(0.05), 5, Inf),
show_group_mapping

cut_labels = c("↓ 1e-5", "↓ 0.05", "non-significant", "↑ 0.05", "↑ 1e-5"),
fill_scale = scale_fill_gradient2(low = "#08A76B", mid = "white", high = "red",
midpoint = ifelse(fill_by_p_value, 0, 1)),
cluster_row = FALSE,
...
)

Arguments

df_enrich  result data.frame from group_enrichment.
return_list if TRUE, return a list of ggplot object so user can combine multiple plots by
other R packages like patchwork.
scales  Should scales be fixed ("fixed", the default), free ("free"), or free in one
dimension ("free_x","free_y")?
add_text_annotation  if TRUE, add text annotation in box. When show p value with filled color, the
text indicates relative change; when show relative change with filled color, the
text indicates p value.
fill_by_p_value  if TRUE, show log10 based p values with filled color. The +/- of p values indicates
change direction. If p vlaues is mapped to fill, then text shows effect size, and
vice versa.
use_fdr  if TRUE, show FDR values instead of raw p-values.
cut_p_value  if TRUE, cut p values into 5 regions for better visualization. Only works when
fill_by_p_value = TRUE.
cut_breaks  when cut_p_value is TRUE, this option set the (log10 based) breaks.
cut_labels  when cut_p_value is TRUE, this option set the labels.
fill_scale  a Scale object generated by ggplot2 package to set color for continuous values.
cluster_row  if TRUE, cluster rows with Hierarchical Clustering (‘complete’ method).
...  other parameters passing to ggplot2::facet_wrap, only used when return_list
is FALSE.

Value

a (list of) ggplot object.

show_group_mapping  Map Groups using Sankey

Description

This feature is designed for signature analysis. However, users can also use it in other similar
situations.
show_group_mapping

Usage

show_group_mapping(
  data,
  col_to_flow,
  cols_to_map,
  include_sig = FALSE,
  fill_na = FALSE,
  title = NULL,
  xlab = NULL,
  ylab = NULL,
  custom_theme = cowplot::theme_minimal_hgrid()
)

Arguments

data a data.frame containing signature group and other categorical groups.
col_to_flow length-1 character showing the column to flow, typically a signature group.
cols_to_map character vector showing colnames of other groups.
include_sig default if FALSE, if TRUE, showing signature group.
fill_na length-1 string to fill NA, default is FALSE.
title the title.
xlab label for x axis.
ylab label for y axis.
custom_theme theme for plotting, default is cowplot::theme_minimal_hgrid().

Value

a ggplot object

Examples

data <- dplyr::tibble(
  Group1 = rep(LETTERS[1:5], each = 10),
  Group2 = rep(LETTERS[6:15], each = 5),
  zzzz = c(rep("xx", 20), rep("yy", 20), rep(NA, 10))
)
p1 <- show_group_mapping(data, col_to_flow = "Group1", cols_to_map = colnames(data)[-1])
p1

p2 <- show_group_mapping(data,
  col_to_flow = "Group1", cols_to_map = colnames(data)[-1],
  include_sig = TRUE
)
p2
show_sig_bootstrap

Show Signature Bootstrap Analysis Results

Description

See details for description.

Usage

show_sig_bootstrap_exposure(
  bt_result,
  sample = NULL,
  signatures = NULL,
  methods = "QP",
  plot_fun = c("boxplot", "violin"),
  agg_fun = c("mean", "median", "min", "max"),
  highlight = "auto",
  highlight_size = 4,
  palette = "aaas",
  title = NULL,
  xlab = FALSE,
  ylab = "Signature exposure",
  width = 0.3,
  dodge_width = 0.8,
  outlier.shape = NA,
  add = "jitter",
  add.params = list(alpha = 0.3),
  ...
)

show_sig_bootstrap_error(
  bt_result,
  sample = NULL,
  methods = "QP",
  plot_fun = c("boxplot", "violin"),
  agg_fun = c("mean", "median"),
  highlight = "auto",
  highlight_size = 4,
  palette = "aaas",
  title = NULL,
  xlab = FALSE,
  ylab = "Reconstruction error (L2 norm)",
  width = 0.3,
  dodge_width = 0.8,
  outlier.shape = NA,
  add = "jitter",
  add.params = list(alpha = 0.3),
  ...
show_sig_bootstrap_stability(
    bt_result,
    signatures = NULL,
    measure = c("RMSE", "CV", "MAE", "AbsDiff"),
    methods = "QP",
    plot_fun = c("boxplot", "violin"),
    palette = "aaas",
    title = NULL,
    xlab = FALSE,
    ylab = "Signature instability",
    width = 0.3,
    outlier.shape = NA,
    add = "jitter",
    add.params = list(alpha = 0.3),
)

Arguments

bt_result           result object from sig_fit_bootstrap_batch.
sample              a sample id.
signatures           signatures to show.
methods             a subset of c("NNLS", "QP", "SA").
plot_fun            set the plot function.
agg_fun             set the aggregation function when sample is NULL.
highlight           set the color for optimal solution. Default is "auto", which use the same color as bootstrap results, you can set it to color like "red", "gold", etc.
highlight_size      size for highlighting triangle, default is 4.
palette             the color palette to be used for coloring or filling by groups. Allowed values include "grey" for grey color palettes; brewer palettes e.g. "RdBu", "Blues", ..; or custom color palette e.g. c("blue", "red"); and scientific journal palettes from ggsci R package, e.g.: "npg", "aaas", "lancet", "jco", "uiscgb", "uchicago", "simpsons" and "rickandmorty".
title               plot main title.
xlab                character vector specifying x axis labels. Use xlab = FALSE to hide xlab.
ylab                character vector specifying y axis labels. Use ylab = FALSE to hide ylab.
width               numeric value between 0 and 1 specifying box width.
dodge_width         dodge width.
outlier.shape       point shape of outlier. Default is 19. To hide outlier, specify outlier.shape = NA. When jitter is added, then outliers will be automatically hidden.
add character vector for adding another plot element (e.g.: dot plot or error bars). Allowed values are one or the combination of: "none", "dotplot", "jitter", "boxplot", "point", "mean", "mean_se", "mean_sd", "mean_ci", "mean_range", "median", "median_iqr", "median_hilow", "median_q1q3", "median_mad", "median_range"; see ?desc_statby for more details.

add.params parameters (color, shape, size, fill, linetype) for the argument 'add'; e.g.: add.params = list(color = "red").

legend character specifying legend position. Allowed values are one of c("top", "bottom", "left", "right", "none"). To remove the legend use legend = "none". Legend position can be also specified using a numeric vector c(x, y); see details section.

measure measure to estimate the exposure instability, can be one of 'RMSE', 'CV', 'MAE' and 'AbsDiff'.

Details

Functions:

- **show_sig_bootstrap_exposure** - this function plots exposures from bootstrap samples with both dotted boxplot. The optimal exposure (the exposure from original input) is shown as triangle point. **Only one sample can be plotted.**

- **show_sig_bootstrap_error** - this function plots decomposition errors from bootstrap samples with both dotted boxplot. The error from optimal solution (the decomposition error from original input) is shown as triangle point. **Only one sample can be plotted.**

- **show_sig_bootstrap_stability** - this function plots the signature exposure instability for specified signatures. Currently, the instability measure supports 3 types:
  - 'RMSE' for Mean Root Squared Error (default) of bootstrap exposures and original exposures for each sample.
  - 'CV' for Coefficient of Variation (CV) based on RMSE (i.e. \( \frac{\text{RMSE}}{\text{btExposure}_{\text{mean}}} \)).
  - 'MAE' for Mean Absolute Error of bootstrap exposures and original exposures for each sample.
  - 'AbsDiff' for Absolute Difference between mean bootstrap exposure and original exposure.

Value

a ggplot object

References


See Also

sig_fit_bootstrap_batch, sig_fit, sig_fit_bootstrap
Examples

```r
if (require("BSgenome.Hsapiens.UCSC.hg19")) {
  laml.maf <- system.file("extdata", "tcga_laml.maf.gz", package = "maftools")
  laml <- read_maf(maf = laml.maf)
  mt_tally <- sig_tally(
    laml,
    ref_genome = "BSgenome.Hsapiens.UCSC.hg19",
    use_syn = TRUE
  )

  library("NMF")
  mt_sig <- sig_extract(mt_tally$nmf_matrix,
    n_sig = 3,
    nrun = 2,
    cores = 1
  )

  mat <- t(mt_tally$nmf_matrix)
  mat <- mat[, colSums(mat) > 0]
  bt_result <- sig_fit_bootstrap_batch(mat, sig = mt_sig, n = 10)
  ## Parallel computation
  ## bt_result = sig_fit_bootstrap_batch(mat, sig = mt_sig, n = 10, use_parallel = TRUE)

  ## At default, mean bootstrap exposure for each sample has been calculated
  p <- show_sig_bootstrap_exposure(bt_result, methods = c("QP"))
  ## Show bootstrap exposure (optimal exposure is shown as triangle)
  p1 <- show_sig_bootstrap_exposure(bt_result, methods = c("QP"), sample = "TCGA-AB-2802")
  p1
  p2 <- show_sig_bootstrap_exposure(bt_result,
    methods = c("QP"),
    sample = "TCGA-AB-3012",
    signatures = c("Sig1", "Sig2")
  )
  p2

  ## Show bootstrap error
  ## Similar to exposure above
  p <- show_sig_bootstrap_error(bt_result, methods = c("QP"))
  p
  p3 <- show_sig_bootstrap_error(bt_result, methods = c("QP"), sample = "TCGA-AB-2802")
  p3

  ## Show exposure (in)stability
  p4 <- show_sig_bootstrap_stability(bt_result, methods = c("QP"))
  p4
  p5 <- show_sig_bootstrap_stability(bt_result, methods = c("QP"), measure = "MAE")
  p5
  p6 <- show_sig_bootstrap_stability(bt_result, methods = c("QP"), measure = "AbsDiff")
  p6
  p7 <- show_sig_bootstrap_stability(bt_result, methods = c("QP"), measure = "CV")
  p7
```
show_sig_consensusmap  

Show Signature Consensus Map

Description

This function is a wrapper of NMF::consensusmap().

Usage

show_sig_consensusmap(
  sig,
  main = "Consensus matrix",
  tracks = c("consensus:", "silhouette:"),
  lab_row = NA,
  lab_col = NA,
  ...
)

Arguments

sig  
a Signature object obtained from sig_extract.

main  
Main title as a character string or a grob.

tracks  
Special additional annotation tracks to highlight associations between basis components and sample clusters:

  basis  
  matches each row (resp. column) to the most contributing basis component in basismap (resp. coefmap). In basismap (resp. coefmap), adding a track ':basis' to annCol (resp. annRow) makes the column (resp. row) corresponding to the component being also highlighted using the matching colours.

lab_row  
labels for the rows.

lab_col  
labels for the columns.

...  
other parameters passing to NMF::consensusmap().

Value

nothing
show_sig_exposure  

Plot Signature Exposure

Description
Currently support copy number signatures and mutational signatures.

Usage

```r
show_sig_exposure(
  Signature,
  sig_names = NULL,
  groups = NULL,
  grp_order = NULL,
  grp_size = NULL,
  cutoff = NULL,
  style = c("default", "cosmic"),
  palette = use_color_style(style),
  base_size = 12,
  font_scale = 1,
  rm_space = FALSE,
  rm_grid_line = TRUE,
  rm_panel_border = FALSE,
  hide_samps = TRUE,
  legend_position = "top"
)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature</td>
<td>a Signature object obtained either from <code>sig_extract</code> or <code>sig_auto_extract</code>, or just a raw absolute exposure matrix with column representing samples (patients) and row representing signatures (signature names must end with different digital numbers, e.g. Sig1, Sig10, x12). If you named signatures with letters, you can specify them by <code>sig_names</code> parameter.</td>
</tr>
<tr>
<td>sig_names</td>
<td>set name of signatures, can be a character vector.</td>
</tr>
<tr>
<td>groups</td>
<td>sample groups, default is NULL.</td>
</tr>
<tr>
<td>grp_order</td>
<td>order of groups, default is NULL.</td>
</tr>
<tr>
<td>grp_size</td>
<td>font size of groups.</td>
</tr>
<tr>
<td>cutoff</td>
<td>a cutoff value to remove hyper-mutated samples.</td>
</tr>
<tr>
<td>style</td>
<td>plot style, one of 'default' and 'cosmic', works when parameter <code>set_gradient_color</code> is FALSE.</td>
</tr>
<tr>
<td>palette</td>
<td>palette used to plot, default use a built-in palette according to parameter <code>style</code>.</td>
</tr>
<tr>
<td>base_size</td>
<td>overall font size.</td>
</tr>
<tr>
<td>font_scale</td>
<td>a number used to set font scale.</td>
</tr>
</tbody>
</table>
show_sig_feature_corrplot

Description

This function is for association visualization. Of note, the parameters `p_val` and `drop` will affect the visualization of association results under p value threshold.
Usage

```
show_sig_feature_corrplot(
  tidy_cor,
  feature_list,
  sort_features = FALSE,
  sig_orders = NULL,
  drop = TRUE,
  return_plotlist = FALSE,
  p_val = 0.05,
  xlab = "Signatures",
  ylab = "Features",
  co_gradient_colors = scale_color_gradient2(low = "blue", mid = "white", high = "red",
                                             midpoint = 0),
  ca_gradient_colors = co_gradient_colors,
  plot_ratio = "auto",
  breaks_count = NULL
)
```

Arguments

tidy_cor data returned by `get_tidy_association`.
feature_list a character vector contains features want to be plotted. If missing, all features will be used.
sort_features default is FALSE, use feature order obtained from the previous step. If TRUE, sort features as feature_list.
sig_orders signature levels for ordering.
drop if TRUE, when a feature has no association with all signatures (p value larger than threshold set by p_val), this feature will be removed from the plot. Otherwise, this feature (a row) will keep with all blank white.
return_plotlist if TRUE, return as a list of ggplot objects.
p_val p value threshold. If p value larger than this threshold, the result becomes blank white.
xlab label for x axis.
ylab label for y axis.
co_gradient_colors a Scale object representing gradient colors used to plot for continuous features.
ca_gradient_colors a Scale object representing gradient colors used to plot for categorical features.
plot_ratio a length-2 numeric vector to set the height/width ratio.
b breaks_count breaks for sample count. If set it to NULL, ggplot bin scale will be used to automatically determine the breaks. If set it to NA, aes for sample will be not used.
show_sig_fit

Value

a ggplot2 object

See Also

get_tidy_association and get_sig_feature_association

Examples

# The data is generated from Wang, Shixiang et al.
load(system.file("extdata", "asso_data.RData", package = "sigminer", mustWork = TRUE))

p <- show_sig_feature_corrplot(
  tidy_data.seqz.feature,
  p_val = 0.05,
  breaks_count = c(0L, 200L, 400L, 600L, 800L, 1020L))
p

desc

desc

Description

See sig_fit for examples.

Usage

show_sig_fit(
  fit_result,
  samples = NULL,
  signatures = NULL,
  plot_fun = c("boxplot", "violin", "scatter"),
  palette = "aaas",
  title = NULL,
  xlab = FALSE,
  ylab = "Signature exposure",
  legend = "none",
  width = 0.3,
  outlier.shape = NA,
  add = "jitter",
  add.params = list(alpha = 0.3),
  ...
)
show_sig_fit

Arguments

**fit_result**
result object from `sig_fit`.

**samples**
samples to show, if `NULL`, all samples are used.

**signatures**
signatures to show.

**plot_fun**
set the plot function.

**palette**
the color palette to be used for coloring or filling by groups. Allowed values include "grey" for grey color palettes; brewer palettes e.g. "RdBu", "Blues", ...; or custom color palette e.g. c("blue", "red"); and scientific journal palettes from ggsci R package, e.g.: "npg", "aaas", "lancet", "jco", "ucscgb", "uchicago", "simpsons" and "rickandmorty".

**title**
plot main title.

**xlab**
character vector specifying x axis labels. Use xlab = FALSE to hide xlab.

**ylab**
character vector specifying y axis labels. Use ylab = FALSE to hide ylab.

**legend**
character specifying legend position. Allowed values are one of c("top", "bottom", "left", "right", "none"). To remove the legend use legend = "none". Legend position can be also specified using a numeric vector c(x, y); see details section.

**width**
numeric value between 0 and 1 specifying box width.

**outlier.shape**
point shape of outlier. Default is 19. To hide outlier, specify outlier.shape = NA. When jitter is added, then outliers will be automatically hidden.

**add**
character vector for adding another plot element (e.g.: dot plot or error bars). Allowed values are one or the combination of: "none", "dotplot", "jitter", "boxplot", "point", "mean", "mean_se", "mean_sd", "mean_ci", "mean_range", "median", "median_iqr", "median_hilow", "median_q1q3", "median_mad", "median_range"; see ?desc_statby for more details.

**add.params**
parameters (color, shape, size, fill, linetype) for the argument 'add'; e.g.: add.params = list(color = "red").

**...**
other arguments to be passed to `geom_boxplot`, `ggpar` and `facet`.

Value

A `ggplot` object.

See Also

`sigFit`, `show_sig_bootstrap_exposure`, `sig_fit_bootstrap`, `sig_fit_bootstrap_batch`
**Description**

Who don’t like to show a barplot for signature profile? This is for it.

**Usage**

```r
show_sig_profile(
  Signature,
  mode = c("SBS", "copynumber", "DBS", "ID", "RS"),
  method = "Wang",
  by_context = FALSE,
  normalize = c("row", "column", "raw", "feature"),
  y_tr = NULL,
  filters = NULL,
  feature_setting = sigminer::CN.features,
  style = c("default", "cosmic"),
  palette = use_color_style(style, ifelse(by_context, "SBS", mode), method),
  set_gradient_color = FALSE,
  free_space = "free_x",
  rm_panel_border = style == "cosmic",
  rm_grid_line = style == "cosmic",
  rm_axis_text = FALSE,
  bar_border_color = ifelse(style == "default", "grey50", "white"),
  bar_width = 0.7,
  paint_axis_text = TRUE,
  x_label_angle = ifelse(mode == "copynumber" & !(startsWith(method, "T") | method == "X"), 60, 90),
  x_label_vjust = ifelse(mode == "copynumber" & !(startsWith(method, "T") | method == "X"), 1, 0.5),
  x_label_hjust = 1,
  x_lab = "Components",
  y_lab = "auto",
  y_limits = NULL,
  params = NULL,
  show_cv = FALSE,
  params_label_size = 3,
  params_label_angle = 60,
  y_expand = 1,
  digits = 2,
  base_size = 12,
  font_scale = 1,
  sig_names = NULL,
  sig_orders = NULL,
  check_sig_names = TRUE
)
Arguments

**Signature**
a Signature object obtained either from `sig_extract` or `sig_auto_extract`, or just a raw signature matrix with row representing components (motifs) and column representing signatures (column names must start with 'Sig').

**mode**
signature type for plotting, now supports 'copynumber', 'SBS', 'DPS', 'ID' and 'RS' (genome rearrangement signature).

**method**
method for copy number feature classification in `sig_tally`, can be one of "Wang" ("W"), "S".

**by_context**
for specific use.

**normalize**
one of 'row', 'column', 'raw' and "feature", for row normalization (signature), column normalization (component), raw data, row normalization by feature, respectively. Of note, 'feature' only works when the mode is 'copynumber'.

**y_tr**
a function (e.g. `log10`) to transform y axis before plotting.

**filters**
a pattern used to select components to plot.

**feature_setting**
a data.frame used for classification. **Only used when method is "Wang"** ("W"). Default is `CN.features`. Users can also set custom input with "feature", "min" and "max" columns available. Valid features can be printed by `unique(CN.features$feature)`.

**style**
plot style, one of 'default' and 'cosmic', works when parameter `set_gradient_color` is FALSE.

**palette**
palette used to plot when `set_gradient_color` is FALSE, default use a built-in palette according to parameter style.

**set_gradient_color**
default is FALSE, if TRUE, use gradient colors to fill bars.

**free_space**
default is 'free_x'. If "fixed", all panels have the same size. If "free_y" their height will be proportional to the length of the y scale; if "free_x" their width will be proportional to the length of the x scale; or if "free" both height and width will vary. This setting has no effect unless the appropriate scales also vary.

**rm_panel_border**
default is TRUE for style 'cosmic', remove panel border to keep plot tight.

**rm_grid_line**
default is FALSE, if TRUE, remove grid lines of plot.

**rm_axis_text**
default is FALSE, if TRUE, remove component texts. This is useful when multiple signature profiles are plotted together.

**bar_border_color**
the color of bar border.

**bar_width**
bar width. By default, set to 70% of the resolution of the data.

**paint_axis_text**
if TRUE, color on text of x axis.

**x_label_angle**
font angle for x label.
`show_sig_profile`

- `x_label_vjust` font vjust for x label.
- `x_label_hjust` font hjust for x label.
- `x_lab` x axis lab.
- `y_lab` y axis lab.
- `y_limits` limits to expand in y axis. e.g., 0.2, c(0, 0.3).
- `params` params data.frame of components, obtained from `sig_tally`.
- `show_cv` default is `FALSE`, if `TRUE`, show coefficient of variation when `params` is not `NULL`.
- `params_label_size` font size for params label.
- `params_label_angle` font angle for params label.
- `y_expand` y expand height for plotting params of copy number signatures.
- `digits` digits for plotting params of copy number signatures.
- `base_size` overall font size.
- `font_scale` a number used to set font scale.
- `sig_names` subset signatures or set name of signatures, can be a character vector. Default is `NULL`, prefix ‘Sig’ plus number is used.
- `sig_orders` set order of signatures, can be a character vector. Default is `NULL`, the signatures are ordered by alphabetical order. If an integer vector set, only specified signatures are plotted.
- `check_sig_names` if `TRUE`, check signature names when input is a matrix, i.e., all signatures (column names) must start with ‘Sig’.

**Value**

a `ggplot` object

**Author(s)**

Shixiang Wang

**See Also**

`show_sig_profile_loop`, `show_sig_profile_heatmap`

**Examples**

```r
# Load SBS signature
load(system.file("extdata", "toy_mutational_signature.RData", 
                  package = "sigminer", mustWork = TRUE)
)
# Show signature profile
p1 <- show_sig_profile(sig2, mode = "SBS")
p1
```
show_sig_profile_heatmap

**Show Signature Profile with Heatmap**

### Description
This is a complementary function to `show_sig_profile()`, it is used for visualizing some big signatures, i.e. SBS-1536, not all signatures are supported. See details for current supported signatures.

### Usage

```r
show_sig_profile_heatmap(
  Signature,
  mode = c("SBS", "DBS"),
  normalize = c("row", "column", "raw"),
  filters = NULL,
  x_lab = NULL,
  y_lab = NULL,
  legend_name = "auto",
  palette = "red",
  x_label_angle = 90,
  x_label_vjust = 1,
  x_label_hjust = 0.5,
  y_label_angle = 0,
```

show_sig_profile_heatmap

y_label_vjust = 0.5,
y_label_hjust = 1,
flip_xy = FALSE,
sig_names = NULL,
sig_orders = NULL,
check_sig_names = TRUE
)

Arguments

Signature  a Signature object obtained either from sig_extract or sig_auto_extract, or just a raw signature matrix with row representing components (motifs) and column representing signatures (column names must start with 'Sig').
mode  one of "SBS" and "DBS".
normalize  one of 'row', 'column', 'raw' and "feature", for row normalization (signature), column normalization (component), raw data, row normalization by feature, respectively. Of note, 'feature' only works when the mode is 'copynumber'.
filters  a pattern used to select components to plot.
x_lab  x label.
y_lab  y label.
legend_name  name of figure legend.
palette  color for value.
x_label_angle  angle for x axis text.
x_label_vjust  vjust for x axis text.
x_label_hjust  hjust for x axis text.
y_label_angle  angle for y axis text.
y_label_vjust  vjust for y axis text.
y_label_hjust  hjust for y axis text.
flip_xy  if TRUE, flip x axis and y axis.
sig_names  subset signatures or set name of signatures, can be a character vector. Default is NULL, prefix 'Sig' plus number is used.
sig_orders  set order of signatures, can be a character vector. Default is NULL, the signatures are ordered by alphabetical order. If an integer vector set, only specified signatures are plotted.
check_sig_names  if TRUE, check signature names when input is a matrix, i.e., all signatures (column names) must start with 'Sig'.

Details

Support:

• SBS-24
• SBS-96
show_sig_profile_loop

- SBS-384
- SBS-1536
- SBS-6144
- DBS-78
- DBS-186

Value

a ggplot object.

Examples

```r
# Load SBS signature
load(system.file("extdata", "toy_mutational_signature.RData", 
    package = "sigminer", mustWork = TRUE))
# Show signature profile
p1 <- show_sig_profile_heatmap(sig2, mode = "SBS")
p1
```

---

**show_sig_profile_loop**  Show Signature Profile with Loop Way

Description

Show Signature Profile with Loop Way

Usage

```r
show_sig_profile_loop(
    Signature, 
    sig_names = NULL, 
    ncol = 1, 
    nrow = NULL, 
    x_lab = "Components", 
    ... 
)
```

Arguments

- **Signature**: a Signature object obtained either from `sig_extract` or `sig_auto_extract`, or just a raw signature matrix with row representing components (motifs) and column representing signatures (column names must start with 'Sig').
- **sig_names**: subset signatures or set name of signatures, can be a character vector. Default is `NULL`, prefix 'Sig' plus number is used.
- **ncol**: (optional) Number of columns in the plot grid.
sigminer

**nrow**  (optional) Number of rows in the plot grid.
**x_lab**  x axis lab.
**...**  other parameters but `sig_order` passing to `show_sig_profile`.

**Value**

aga plot result from `cowplot::plot_grid()`.

**See Also**

`show_sig_profile`

**Examples**

```r
load(system.file("extdata", "toy_mutational_signature.RData", package = "sigminer", mustWork = TRUE))

# Show signature profile
p1 <- show_sig_profile_loop(sig2, mode = "SBS")
p1
p2 <- show_sig_profile_loop(sig2, mode = "SBS", style = "cosmic", sig_names = c("A", "B", "C"))
p2
```
sigprofiler

Extract Signatures with SigProfiler

Description

This function provides an interface to software SigProfiler. More please see https://github.com/AlexandrovLab/SigProfilerExtractor. Typically, a reference genome is not required because the input is a matrix (my understanding).

Usage

```r
sigprofiler_extract(
  nmf_matrix,
  output,
  range = 2:5,
  nrun = 10L,
  refit = FALSE,
  refit_plot = FALSE,
  is_exome = FALSE,
  init_method = c("nndsvd_min", "random", "alexandrov-lab-custom", "nndsvd", "nndsvda", "nndsvdar"),
  cores = -1L,
  genome_build = c("hg19", "hg38", "mm10", "mm9"),
  use_conda = FALSE,
  py_path = NULL,
  sigprofiler_version = "1.1.3"
)
```

```r
sigprofiler_import(
  output,
  order_by_expo = FALSE,
  type = c("suggest", "refit", "all")
)
```

Arguments

- **nmf_matrix**: a matrix used for NMF decomposition with rows indicate samples and columns indicate components.
- **output**: output directory.
- **range**: signature number range, i.e. 2:5.
- **nrun**: the number of iteration to be performed to extract each signature number.
- **refit**: if TRUE, then refit the denovo signatures with nnls. Same meaning as optimize option in sig_extract or sig_auto_extract.
- **refit_plot**: if TRUE, SigProfiler will make denovo to COSMIC sigantures decompostion plots. However, this may fail due to some matrix cannot be identified by SigProfiler plot program.
sig_auto_extract

is_exome if TRUE, the exomes will be extracted.
init_method the initialization algorithm for W and H matrix of NMF. Options are 'random', 'nndsvd', 'nndsvda', 'nndsvdar', 'alexandrov-lab-custom' and 'nndsvd_min'.
cores number of cores used for computation.
genome_build I think this option is useless when input is matrix, keep it in case it is useful.
use_conda if TRUE, create an independent conda environment to run SigProfiler.
py_path path to Python executable file, e.g. '/Users/wsx/anaconda3/bin/python'.
sigprofiler_version version of SigProfilerExtractor. If this package is not installed, the specified package will be installed. If this package is installed, this option is useless.
order_by_expo if TRUE, order the import signatures by their exposures, e.g. the signature contributed the most exposure in all samples will be named as Sig1.
type one of 'suggest' (for suggested solution), 'refit' (for refit solution) or 'all' (for all solutions).

Value

For sigprofiler_extract(), returns nothing. See output directory.
For sigprofiler_import(), a list containing Signature object.

Examples

```r
if (FALSE) {
  load(system.file("extdata", "toy_copynumber_tally_W.RData", package = "sigminer", mustWork = TRUE
})

reticulate::conda_list()

sigprofiler_extract(cn_tally_W$nmf_matrix, "/test/test_sigminer",
  use_conda = TRUE
}

sigprofiler_extract(cn_tally_W$nmf_matrix, "/test/test_sigminer",
  use_conda = FALSE, py_path = "/Users/wsx/anaconda3/bin/python"
}
```
Description

A bayesian variant of NMF algorithm to enable optimal inferences for the number of signatures through the automatic relevance determination technique. This functions delevers highly interpretable and sparse representations for both signature profiles and attributions at a balance between data fitting and model complexity (this method may introduce more signatures than expected, especially for copy number signatures (thus I don’t recommend you to use this feature to extract copy number signatures)). See detail part and references for more.

Usage

```r
sig_auto_extract(
  nmf_matrix = NULL,
  result_prefix = "BayesNMF",
  destdir = tempdir(),
  method = c("L1W.L2H", "L1KL", "L2KL"),
  strategy = c("stable", "optimal", "ms"),
  ref_sigs = NULL,
  K0 = 25,
  nrun = 10,
  niter = 2e+05,
  tol = 1e-07,
  cores = 1,
  optimize = FALSE,
  skip = FALSE,
  recover = FALSE
)
```

Arguments

- `nmf_matrix`: a matrix used for NMF decomposition with rows indicate samples and columns indicate components.
- `result_prefix`: prefix for result data files.
- `destdir`: path to save data runs, default is `tempdir()`.
- `method`: default is "L1W.L2H", which uses an exponential prior for W and a half-normal prior for H (This method is used by PCAWG project, see reference #3). You can also use "L1KL" to set exponential priors for both W and H, and "L2KL" to set half-normal priors for both W and H. The latter two methods are originally implemented by SignatureAnalyzer software.
- `strategy`: the selection strategy for returned data. Set 'stable' for getting optimal result from the most frequent K. Set 'optimal' for getting optimal result from all Ks. Set 'ms' for getting result with maximum mean cosine similarity with provided reference signatures. See `ref_sigs` option for details. If you want select other solution, please check `get_bayesian_result`.
- `ref_sigs`: A Signature object or matrix or string for specifying reference signatures, only used when `strategy = 'ms'`. See Signature and `sig_db` options in `get_sig_similarity` for details.
- `K0`: number of initial signatures.
nrun  
number of independent simulations.

niter  
the maximum number of iterations.

tol  
tolerance for convergence.

cores  
number of cpu cores to run NMF.

optimize  
if TRUE, then refit the denovo signatures with QP method, see sig_fit.

skip  
if TRUE, it will skip running a previous stored result. This can be used to extend run times, e.g. you try running 10 times firstly and then you want to extend it to 20 times.

recover  
if TRUE, try to recover result from previous runs based on input result_prefix, destdir and nrun. This is pretty useful for reproducing result. Please use skip if you want to recover an unfinished job.

Details

There are three methods available in this function: "L1W.L2H", "L1KL" and "L2KL". They use different priors for the bayesian variant of NMF algorithm (see method parameter) written by reference #1 and implemented in SignatureAnalyzer software (reference #2).

I copied source code for the three methods from Broad Institute and supplementary files of reference #3, and wrote this higher function. It is more friendly for users to extract, visualize and analyze signatures by combining with other powerful functions in sigminer package. Besides, I implemented parallel computation to speed up the calculation process and a similar input and output structure like sig_extract().

Value

a list with Signature class.

Author(s)

Shixiang Wang

References


See Also

sig_tally for getting variation matrix, sig_extract for extracting signatures using NMF package, sig_estimate for estimating signature number for sig_extract.
Examples

```r
load(system.file("extdata", "toy_copynumber_tally_W.RData", package = "sigminer", mustWork = TRUE))
res <- sig_auto_extract(cn_tally_W$nmf_matrix, result_prefix = "Test_copynumber", nrun = 1)
# At default, all run files are stored in tempdir()
dir(tempdir(), pattern = "Test_copynumber")

laml.maf <- system.file("extdata", "tcga_laml.maf.gz", package = "maftools")
laml <- read_maf(maf = laml.maf)
mt_tally <- sig_tally(
  laml,
  ref_genome = "BSgenome.Hsapiens.UCSC.hg19",
  use_syn = TRUE
)
x <- sig_auto_extract(mt_tally$nmf_matrix,
  strategy = "ms", nrun = 3, ref_sigs = "legacy"
)
x
```

---

**sig_convert**  
*Convert Signatures between different Genomic Distribution of Components*

**Description**

Converts signatures between two representations relative to different sets of mutational opportunities. Currently, only SBS signature is supported.

**Usage**

```r
sig_convert(sig, from = "human-genome", to = "human-exome")
```

**Arguments**

- **sig**  
  A Signature object obtained either from `sig_extract` or `sig_auto_extract`, or just a raw signature matrix/data.frame with row representing components (motifs) and column representing signatures.

- **from**  
  Either one of "human-genome" and "human-exome" or an opportunity matrix (repeated n columns with each row represents the total number of mutations for a component, n is the number of signature).

- **to**  
  Same as from.

**Details**

The default opportunity matrix for "human-genome" and "human-exome" comes from COSMIC signature database v2 and v3.
Value

a matrix.

References

convert_signatures function from sigfit package.

Examples

# Load SBS signature
load(system.file("extdata", "toy_mutational_signature.RData",
    package = "sigminer", mustWork = TRUE
))
# Exome-relative to Genome-relative
sig_converted <- sig_convert(sig2,
    from = "human-exome",
    to = "human-genome"
)
sig_converted

show_sig_profile(sig2, style = "cosmic")
show_sig_profile(sig_converted, style = "cosmic")

Description

Use NMF package to evaluate the optimal number of signatures. This is used along with sig_extract. Users should library(NMF) firstly. If NMF objects are returned, the result can be further visualized by NMF plot methods like NMF::consensusmap() and NMF::basismap().

sig_estimate() shows comprehensive rank survey generated by NMF package, sometimes it is hard to consider all measures. show_sig_number_survey() provides a one or two y-axis visualization method to help users determine the optimal signature number (showing both stability ("cophenetic") and error (RSS) at default). Users can also set custom measures to show.

show_sig_number_survey2() is modified from NMF package to better help users to explore survey of signature number.

Usage

sig_estimate(
    nmf_matrix,
    range = 2:5,
    nrun = 10,
    use_random = FALSE,
    method = "brunet",
    seed = 123456,
sig_estimate

```r
cores = 1,
keep_nmfObj = FALSE,
save_plots = FALSE,
plot_basename = file.path(tempdir(), "nmf"),
what = "all",
verbose = FALSE
)

show_sig_number_survey(
  object,
  x = "rank",
  left_y = "cophenetic",
  right_y = "rss",
  left_name = left_y,
  right_name = toupper(right_y),
  left_color = "black",
  right_color = "red",
  left_shape = 16,
  right_shape = 18,
  shape_size = 4,
  highlight = NULL
)

show_sig_number_survey2(
  x,
  y = NULL,
  what = c("all", "cophenetic", "rss", "residuals", "dispersion", "evar", "sparseness",
            "sparseness.basis", "sparseness.coef", "silhouette", "silhouette.coef",
            "silhouette.basis", "silhouette.consensus"),
  na.rm = FALSE,
  xlab = "Total signatures",
  ylab = "",
  main = "Signature number survey using NMF package"
)
```

**Arguments**

- `nmf_matrix` a matrix used for NMF decomposition with rows indicate samples and columns indicate components.
- `range` a numeric vector containing the ranks of factorization to try. Note that duplicates are removed and values are sorted in increasing order. The results are notably returned in this order.
- `nrun` a numeric giving the number of run to perform for each value in `range`, `nrun` set to 30–50 is enough to achieve robust result.
- `use_random` Should generate random data from input to test measurements. Default is TRUE.
- `method` specification of the NMF algorithm. Use 'brunet' as default. Available methods for NMF decompositions are 'brunet', 'lee', 'ls-nmf', 'nsNMF', 'offset'.
**seed** specification of the starting point or seeding method, which will compute a starting point, usually using data from the target matrix in order to provide a good guess.

**cores** number of cpu cores to run NMF.

**keep_nmfObj** default is FALSE, if TRUE, keep NMF objects from runs, and the result may be huge.

**save_plots** if TRUE, save signature number survey plot to local machine.

**plot_basename** when save plots, set custom basename for file path.

**what** a character vector whose elements partially match one of the following item, which correspond to the measures computed by `summary()` on each multi-run NMF result: 'all', 'cophenetic', 'rss', 'residuals', 'dispersion', 'evar', 'silhouette' (and more specific *.coef, *.basis, *.consensus), 'sparseness' (and more specific *.coef, *.basis). It specifies which measure must be plotted (what='all' plots all the measures).

**verbose** if TRUE, print extra message.

**object** a Survey object generated from `sig_estimate`, or a data.frame contains at least rank columns and columns for one measure.

**x** a data.frame or NMF.rank object obtained from `sig_estimate()`.

**left_y** column name for left y axis.

**right_y** column name for right y axis.

**left_name** label name for left y axis.

**right_name** label name for right y axis.

**left_color** color for left axis.

**right_color** color for right axis.

**left_shape**, **right_shape**, **shape_size** shape setting.

**highlight** a integer to highlight a x.

**y** for random simulation, a data.frame or NMF.rank object obtained from `sig_estimate()`.

**na.rm** single logical that specifies if the rank for which the measures are NA values should be removed from the graph or not (default to FALSE). This is useful when plotting results which include NAs due to error during the estimation process. See argument `stop` for nmfEstimateRank.

**xlab** x-axis label

**ylab** y-axis label

**main** main title

**Details**

The most common approach is to choose the smallest rank for which cophenetic correlation coefficient starts decreasing (Used by this function). Another approach is to choose the rank for which the plot of the residual sum of squares (RSS) between the input matrix and its estimate shows an inflection point. More custom features please directly use `NMF::nmfEstimateRank`. 

```r
sig_estimate
```
Value

- `sig_estimate`: a list contains information of NMF run and rank survey.
- `show_sig_number_survey`: a ggplot object
- `show_sig_number_survey2`: a ggplot object

Author(s)

Shixiang Wang

References


See Also

- `sig_extract` for extracting signatures using NMF package, `sig_auto_extract` for extracting signatures using automatic relevance determination technique.
- `sig_estimate` for estimating signature number for `sig_extract`, `show_sig_number_survey2` for more visualization method.

Examples

```r
load(system.file("extdata", "toy_copynumber_tally_W.RData", package = "sigminer", mustWork = TRUE))
library(NMF)
cn_estimate <- sig_estimate(cn_tally_W$nmf_matrix, cores = 1, nrun = 5, verbose = TRUE)

p <- show_sig_number_survey2(cn_estimate$survey)
p

# Show two measures
show_sig_number_survey(cn_estimate)
# Show one measure
p1 <- show_sig_number_survey(cn_estimate, right_y = NULL)
p1
p2 <- add_h_arrow(p, x = 4.1, y = 0.953, label = "selected number")
p2

# Show data from a data.frame
p3 <- show_sig_number_survey(cn_estimate$survey)
p3
# Show other measures
head(cn_estimate$survey)
```
sig_extract

Extract Signatures through NMF

Description

Do NMF de-composition and then extract signatures.

Usage

sig_extract(
  nmf_matrix,  # a matrix used for NMF decomposition with rows indicate samples and columns indicate components.
  n_sig,       # number of signature. Please run sig_estimate to select a suitable value.
  nrun = 10,   # a numeric giving the number of run to perform for each value in range, nrun set to 30-50 is enough to achieve robust result.
  cores = 1,   # number of cpu cores to run NMF.
  method = "brunet",  # specification of the NMF algorithm. Use 'brunet' as default. Available methods for NMF decompositions are 'brunet', 'lee', 'ls-nmf', 'nsNMF', 'offset'.
  optimize = FALSE,  # if TRUE, then refit the denovo signatures with QP method, see sig_fit.
  ...)

Arguments

nmf_matrix        a matrix used for NMF decomposition with rows indicate samples and columns indicate components.

n_sig            number of signature. Please run sig_estimate to select a suitable value.

nrun            a numeric giving the number of run to perform for each value in range, nrun set to 30-50 is enough to achieve robust result.

cores            number of cpu cores to run NMF.

method            specification of the NMF algorithm. Use 'brunet' as default. Available methods for NMF decompositions are 'brunet', 'lee', 'ls-nmf', 'nsNMF', 'offset'.

optimize            if TRUE, then refit the denovo signatures with QP method, see sig_fit.
if TRUE, use Python NMF driver Nimfa. The seed currently is not used by this implementation.

if TRUE, create an independent conda environment to run NMF.

path to Python executable file, e.g. '/Users/wsx/anaconda3/bin/python'. In my test, it is more stable than use_conda=TRUE. You can install the Nimfa package by yourself or set use_conda to TRUE to install required Python environment, and then set this option.

specification of the starting point or seeding method, which will compute a starting point, usually using data from the target matrix in order to provide a good guess.

other arguments passed to NMF::nmf().

a list with Signature class.

Shixiang Wang


sig_tally for getting variation matrix, sig_estimate for estimating signature number for sig_extract, sig_auto_extract for extracting signatures using automatic relevance determination technique.

load(system.file("extdata", "toy_copynumber_tally_W.RData", package = "sigminer", mustWork = TRUE))

# Extract copy number signatures
res <- sig_extract(cn_tally_W$nmf_matrix, 2, nrun = 1)
**Description**

The function performs a signatures decomposition of a given mutational catalogue \( V \) with known signatures \( W \) by solving the minimization problem \( \min(||W*H - V||) \) where \( W \) and \( V \) are known.

**Usage**

```r
sig_fit(
  catalogue_matrix,
  sig,
  sig_index = NULL,
  sig_db = c("legacy", "SBS", "DBS", "ID", "TSB", "SBS_Nik_lab", "RS_Nik_lab", "RS_BRCA560", "RS_USARC", "CNS_USARC", "CNS_TCGA", "SBS_hg19", "SBS_hg38", "SBS_mm9", "SBS_mm10", "DBS_hg19", "DBS_hg38", "DBS_mm9", "DBS_mm10", "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "latest_SBS_GRCh37", "latest_DBs_GRCh37", "latest_ID_GRCh37", "latest_SBS_GRCh38", "latest_DBs_GRCh38", "latest_SBS_mm9", "latest_DBs_mm9", "latest_SBS_mm10", "latest_DBs_mm10", "latest_SBS_rn6", "latest_DBs_rn6"),
  db_type = c("", "human-exome", "human-genome"),
  show_index = TRUE,
  method = c("QP", "NNLS", "SA"),
  auto_reduce = FALSE,
  type = c("absolute", "relative"),
  return_class = c("matrix", "data.table"),
  return_error = FALSE,
  rel_threshold = 0,
  mode = c("SBS", "DBS", "ID", "copynumber"),
  true_catalog = NULL,
  ...
)
```

**Arguments**

- **catalogue_matrix**
  a numeric matrix \( V \) with row representing components and columns representing samples, typically you can get \( \text{nmf_matrix} \) from \text{sig_tally()} and transpose it by \( t() \).

- **sig**
  a Signature object obtained either from \text{sig_extract} or \text{sig_auto_extract}, or just a raw signature matrix/data.frame with row representing components (motifs) and column representing signatures.

- **sig_index**
  a vector for signature index. "ALL" for all signatures.

- **sig_db**
  default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9',...
'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. **UPDATE**, the latest version of reference version can be automatically downloaded and loaded from https://cancer.sanger.ac.uk/signatures/downloads/ when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). **Note**: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

db_type only used when sig_db is enabled. "" for keeping default, "human-exome" for transforming to exome frequency of component, and "human-genome" for transforming to whole genome frequency of component. Currently only works for 'SBS'.

show_index if TRUE, show valid indices.

method method to solve the minimazation problem. 'NNLS' for non-negative least square; 'QP' for quadratic programming; 'SA' for simulated annealing.

auto_reduce if TRUE, try reducing the input reference signatures to increase the cosine similarity of reconstructed profile to observed profile.

type 'absolute' for signature exposure and 'relative' for signature relative exposure.

return_class string, 'matrix' or 'data.table'.

return_error if TRUE, also return sample error (Frobenius norm) and cosine similarity between observed sample profile (asa. spectrum) and reconstructed profile. **NOTE**: it is better to obtain the error when the type is 'absolute', because the error is affected by relative exposure accuracy.

rel_threshold numeric vector, a signature with relative exposure lower than (equal is included, i.e. <=) this value will be set to 0 (both absolute exposure and relative exposure). In this case, sum of signature contribution may not equal to 1.

mode signature type for plotting, now supports 'copynumber', 'SBS', 'DBS', 'ID' and 'RS' (genome rearrangement signature).

true_catalog used by sig_fit_bootstrap, user never use it.

... control parameters passing to argument control in GenSA function when use method 'SA'.

**Details**

The method 'NNLS' solves the minimization problem with nonnegative least-squares constraints. The method 'QP' and 'SA' are modified from SignatureEstimation package. See references for details. Of note, when fitting exposures for copy number signatures, only components of feature CN is used.
Value

The exposure result either in matrix or data.table format. If return_error set TRUE, a list is returned.

References


See Also

sig_extract, sig_auto_extract, sig_fit_bootstrap, sig_fit_bootstrap_batch

Examples

```
W <- matrix(c(1, 2, 3, 4, 5, 6), ncol = 2)
colnames(W) <- c("sig1", "sig2")
W <- apply(W, 2, function(x) x / sum(x))
H <- matrix(c(2, 5, 3, 6, 1, 9, 1, 2), ncol = 4)
colnames(H) <- paste0("samp", 1:4)
V <- W %*% H
V

if (requireNamespace("quadprog", quietly = TRUE)) {
  H_infer <- sig_fit(V, W, method = "QP")
  H_infer
  H

  H_dt <- sig_fit(V, W, method = "QP", auto_reduce = TRUE, return_class = "data.table")
  H_dt

  ## Show results
  show_sig_fit(H_infer)
  show_sig_fit(H_dt)

  ## Get clusters/groups
  H_dt_rel <- sig_fit(V, W, return_class = "data.table", type = "relative")
  z <- get_groups(H_dt_rel, method = "k-means")
  show_groups(z)
}
```

# if (requireNamespace("GenSA", quietly = TRUE)) {
#   H_infer <- sig_fit(V, W, method = "SA")
#   H_infer
#   H
```
# H_dt <- sig_fit(V, W, method = "SA", return_class = "data.table")
# H_dt
#
# ## Modify arguments to method
# sig_fit(V, W, method = "SA", maxit = 10, temperature = 100)
#
# ## Show results
# show_sig_fit(H_infer)
# show_sig_fit(H_dt)
#

---

**sig_fit_bootstrap**

*Obtain Bootstrap Distribution of Signature Exposures of a Certain Tumor Sample*

**Description**

This can be used to obtain the confidence of signature exposures or search the suboptimal decomposition solution.

**Usage**

```r
sig_fit_bootstrap(
  catalog,
  sig,
  n = 100L,
  sig_index = NULL,
  sig_db = "legacy",
  db_type = c("", "human-exome", "human-genome"),
  show_index = TRUE,
  method = c("QP", "NNLS", "SA"),
  auto_reduce = FALSE,
  SA_not_bootstrap = FALSE,
  type = c("absolute", "relative"),
  rel_threshold = 0,
  mode = c("SBS", "DBS", "ID", "copynumber"),
  find_suboptimal = FALSE,
  suboptimal_ref_error = NULL,
  suboptimal_factor = 1.05,
  ...
)
```

**Arguments**

- `catalog` a named numeric vector or a numeric matrix with dimension N x 1. N is the number of component, 1 is the sample.
sig

a Signature object obtained either from `sig_extract` or `sig_auto_extract`, or just a raw signature matrix/data.frame with row representing components (motifs) and column representing signatures.

n

the number of bootstrap replicates.

sig_index

a vector for signature index. "ALL" for all signatures.

sig_db

default 'legacy', it can be 'legacy' (for COSMIC v2 'SBS'), 'SBS', 'DBS', 'ID' and 'TSB' (for COSMIV v3.1 signatures) for small scale mutations. For more specific details, it can also be 'SBS_hg19', 'SBS_hg38', 'SBS_mm9', 'SBS_mm10', 'DBS_hg19', 'DBS_hg38', 'DBS_mm9', 'DBS_mm10' to use COSMIC v3 reference signatures from Alexandrov, Ludmil B., et al. (2020) (reference #1). In addition, it can be one of "SBS_Nik_lab_Organ", "RS_Nik_lab_Organ", "SBS_Nik_lab", "RS_Nik_lab" to refer reference signatures from Degasperi, Andrea, et al. (2020) (reference #2); "RS_BRCA560", "RS_USARC" to reference signatures from BRCA560 and USARC cohorts; "CNS_USARC" (40 categories), "CNS_TCGA" (48 categories) to reference copy number signatures from USARC cohort and TCGA. UPDATE, the latest version of reference version can be automatically downloaded and loaded from https://cancer.sanger.ac.uk/signatures/downloads/ when a option with latest_prefix is specified (e.g. "latest_SBS_GRCh37"). Note: the signature profile for different genome builds are basically same. And specific database (e.g. 'SBS_mm10') contains less signatures than all COSMIC signatures (because some signatures are not detected from Alexandrov, Ludmil B., et al. (2020)). For all available options, check the parameter setting.

db_type

only used when sig_db is enabled. "" for keeping default, "human-exome" for transforming to exome frequency of component, and "human-genome" for transforming to whole genome frequency of component. Currently only works for 'SBS'.

show_index

if TRUE, show valid indices.

method

method to solve the minimazation problem. 'NNLS' for non-negative least square; 'QP' for quadratic programming; 'SA' for simulated annealing.

auto_reduce

if TRUE, try reducing the input reference signatures to increase the cosine similarity of reconstructed profile to observed profile.

SA_not_bootstrap

if TRUE, directly run 'SA' multiple times with original input instead of bootstrap samples.

type

'absolute' for signature exposure and 'relative' for signature relative exposure.

rel_threshold

numeric vector, a signature with relative exposure lower than (equal is included, i.e. <=) this value will be set to 0 (both absolute exposure and relative exposure). In this case, sum of signature contribution may not equal to 1.

mode

signature type for plotting, now supports 'copynumber', 'SBS', 'DBS', 'ID' and 'RS' (genome rearrangement signature).

find_suboptimal

logical, if TRUE, find suboptimal decomposition with slightly higher error than the optimal solution by method 'SA'. This is useful to explore hidden dependencies between signatures. More see reference.
suboptimal_ref_error
baseline error used for finding suboptimal solution. If it is NULL, then use 'SA'
method to obtain the optimal error.

suboptimal_factor
suboptimal factor to get suboptimal error, default is 1.05, i.e., suboptimal error
is 1.05 times baseline error.

... control parameters passing to argument control in GenSA function when use
method 'SA'.

Value
a list

References
Huang X, Wojtowicz D, Przytycka TM. Detecting presence of mutational signatures in cancer with

See Also
report_bootstrap_p_value, sig_fit, sig_fit_bootstrap_batch

Examples
W <- matrix(c(1, 2, 3, 4, 5, 6), ncol = 2)
colnames(W) <- c("sig1", "sig2")
W <- apply(W, 2, function(x) x / sum(x))

H <- matrix(c(2, 5, 3, 6, 1, 9, 1, 2), ncol = 4)
colnames(H) <- paste0("samp", 1:4)

V <- W %*% H

if (requireNamespace("quadprog", quietly = TRUE)) {
  H_bootstrap <- sig_fit_bootstrap(V[, 1], W, n = 10, type = "absolute")
  ## Typically, you have to run many times to get close to the answer
  boxplot(t(H_bootstrap$expo))
  H[, 1]
  ## Return P values
  ## In practice, run times >= 100
  ## is recommended
  report_bootstrap_p_value(H_bootstrap)
  ## For multiple samples
  ## Input a list
  report_bootstrap_p_value(list(samp1 = H_bootstrap, samp2 = H_bootstrap))

  #  ## Find suboptimal decomposition
  #  H_suboptimal <- sig_fit_bootstrap(V[, 1], W,
  #  n = 10,}
sig_fit_bootstrap_batch

Exposure Instability Analysis of Signature Exposures with Bootstrapping

Description

Read sig_fit_bootstrap for more option setting.

Usage

```r
sig_fit_bootstrap_batch(
  catalogue_matrix,
  methods = c("QP"),
  n = 100L,
  min_count = 1L,
  p_val_thresholds = c(0.05),
  use_parallel = FALSE,
  seed = 123456L,
  job_id = NULL,
  result_dir = tempdir(),
  ...
)
```

Arguments

- `catalogue_matrix`:
  a numeric matrix $V$ with row representing components and columns representing samples, typically you can get `nmf_matrix` from `sig_tally()` and transpose it by `t()`.

- `methods`:
  a subset of `c("NNLS", "QP", "SA")`.

- `n`:
  the number of bootstrap replicates.

- `min_count`:
  minimal exposure in a sample, default is 1. Any patient has total exposure less than this value will be filtered out.

- `p_val_thresholds`:
  a vector of relative exposure threshold for calculating $p$ values.

- `use_parallel`:
  if `TRUE`, use parallel computation based on `furrr` package. It can also be an integer for specifying cores.

- `seed`:
  random seed to reproduce the result.
**job_id**

A job ID, default is NULL, can be a string. When not NULL, all bootstrapped results will be saved to local machine location defined by `result_dir`. This is very useful for running more than 10 times for more than 100 samples.

**result_dir**

See above, default is temp directory defined by R.

... other common parameters passing to `sig_fit_bootstrap`, including `sig`, `sig_index`, `sig_db`, `db_type`, `mode`, `auto_reduce` etc.

**Value**

A list of `data.table`.

**See Also**

`sig_fit`, `sig_fit_bootstrap`

**Examples**

```r
W <- matrix(c(1, 2, 3, 4, 5, 6), ncol = 2)
colnames(W) <- c("sig1", "sig2")
W <- apply(W, 2, function(x) x / sum(x))

H <- matrix(c(2, 5, 3, 6, 1, 9, 1, 2), ncol = 4)
colnames(H) <- paste0("samp", 1:4)

V <- W %*% H
V

if (requireNamespace("quadprog")) {
  z10 <- sig_fit_bootstrap_batch(V, sig = W, n = 10)
  z10
}
```

---

**Get or Modify Signature Information**

**Description**

Obtain or modify signature information.

**Usage**

- `sig_names(sig)`
- `sig_modify_names(sig, new_names)`
- `sig_number(sig)`
- `sig_attrs(sig)`
sig_signature(sig, normalize = c("row", "column", "raw", "feature"))

sig_exposure(sig, type = c("absolute", "relative"))

**Arguments**

- **sig**
  - a Signature object obtained either from `sig_extract` or `sig_auto_extract`.
- **new_names**
  - new signature names.
- **normalize**
  - one of 'row', 'column', 'raw' and "feature", for row normalization (signature), column normalization (component), raw data, row normalization by feature, respectively.
- **type**
  - one of 'absolute' and 'relative'.

**Value**

a Signature object or data.

**Examples**

```r
## Operate signature names
load(system.file("extdata", "toy_mutational_signature.RData", package = "sigminer", mustWork = TRUE))
sig_names(sig2)
cc <- sig_modify_names(sig2, new_names = c("Sig2", "Sig1", "Sig3"))
sig_names(cc)

# The older names are stored in tags.
print(attr(cc, "tag"))
## Get signature number
sig_number(sig2)
## Get signature attributes
sig_number(sig2)
## Get signature matrix
z <- sig_signature(sig2)
z <- sig_signature(sig2, normalize = "raw")
## Get exposure matrix
## Of note, this is different from get_sig_exposure()
## it returns a matrix instead of data table.
z <- sig_exposure(sig2) # it is same as sig$Exposure
z <- sig_exposure(sig2, type = "relative") # it is same as sig2$Exposure.norm
```

---

**sig_tally**

Tally a Genomic Alteration Object
Description

Tally a variation object like MAF, CopyNumber and return a matrix for NMF de-composition and more. This is a generic function, so it can be further extended to other mutation cases. Please read details about how to set sex for identifying copy number signatures. Please read https://osf.io/s93d5/ for the generation of SBS, DBS and ID (INDEL) components.

Usage

sig_tally(object, ...)

## S3 method for class 'CopyNumber'

sig_tally(
  object,
  method = "Wang",
  ignore_chrs = NULL,
  indices = NULL,
  add_loh = FALSE,
  feature_setting = sigminer::CN.features,
  cores = 1,
  keep_only_matrix = FALSE,
...
)

## S3 method for class 'RS'

sig_tally(object, keep_only_matrix = FALSE, ...)

## S3 method for class 'MAF'

sig_tally(
  object,
  mode = c("SBS", "DBS", "ID", "ALL"),
  ref_genome = "BSgenome.Hsapiens.UCSC.hg19",
  genome_build = NULL,
  add_trans_bias = FALSE,
  ignore_chrs = NULL,
  use_syn = TRUE,
  keep_only_matrix = FALSE,
...
)

Arguments

object a CopyNumber object or MAF object or SV object (from read_sv_as_rs).

... custom setting for operating object. Detail see S3 method for corresponding class (e.g. CopyNumber).

method method for feature classification, can be one of "Wang" ("W"), "S" (for method described in Steele et al. 2019).

ignore_chrs Chromosomes to ignore from analysis. e.g. chrX and chrY.
Indices integer vector indicating segments to keep.

Add_loh flag to add LOH classifications.

Feature_setting a data.frame used for classification. Only used when method is "Wang" ("W"). Default is CN.features. Users can also set custom input with "feature", "min" and "max" columns available. Valid features can be printed by unique(CN.features$feature).

Cores number of computer cores to run this task. You can use future::availableCores() function to check how many cores you can use.

Keep_only_matrix if TRUE, keep only matrix for signature extraction. For a MAF object, this will just return the most useful matrix.

Mode type of mutation matrix to extract, can be one of 'SBS', 'DBS' and 'ID'.

Ref_genome 'BSgenome.Hsapiens.UCSC.hg19', 'BSgenome.Hsapiens.UCSC.hg38', 'BSgenome.Mmusculus.UCSC.mm10', 'BSgenome.Mmusculus.UCSC.mm9', etc.

Genome_build genome build 'hg19', 'hg38', 'mm9' or "mm10", if not set, guess it by ref_genome.

Add_trans_bias if TRUE, consider transcriptional bias categories. 'T:' for Transcribed (the variant is on the transcribed strand); 'U:' for Un-transcribed (the variant is on the untranscribed strand); 'B:' for Bi-directional (the variant is on both strand and is transcribed either way); 'N:' for Non-transcribed (the variant is in a non-coding region and is untranslated); 'Q:' for Questionable. NOTE: the result counts of 'B' and 'N' labels are a little different from SigProfilerMatrixGenerator, the reason is unknown (may be caused by annotation file).

Use_syn Logical. If TRUE, include synonymous variants in analysis.

Details

For identifying copy number signatures, we have to derive copy number features firstly. Due to the difference of copy number values in sex chromosomes between male and female, we have to do an extra step if we don’t want to ignore them.

I create two options to control this, the default values are shown as the following, you can use the same way to set (per R session).

options(sigminer.sex = "female", sigminer.copynumber.max = NA_integer_)

• If your cohort are all females, you can totally ignore this.

• If your cohort are all males, set sigminer.sex to 'male' and sigminer.copynumber.max to a proper value (the best is consistent with read_copynumber).

• If your cohort contains both males and females, set sigminer.sex as a data.frame with two columns "sample" and "sex". And set sigminer.copynumber.max to a proper value (the best is consistent with read_copynumber).

Value

A list contains a matrix used for NMF de-composition.
Methods (by class)

- CopyNumber: Returns copy number features, components and component-by-sample matrix
- RS: Returns genome rearrangement sample-by-component matrix
- MAF: Returns SBS mutation sample-by-component matrix and APOBEC enrichment

Author(s)

Shixiang Wang

References


See Also

sig_estimate for estimating signature number for sig_extract, sig_auto_extract for extracting signatures using automatic relevance determination technique.

Examples

```r
# Load copy number object
load(system.file("extdata", "toy_copynumber.RData", 
    package = "sigminer", mustWork = TRUE ))

# Use method designed by Wang, Shixiang et al.
cn_tally_W <- sig_tally(cn, method = "W")

# Use method designed by Steele et al.
# See example in read_copynumber

# Prepare SBS signature analysis
laml.maf <- system.file("extdata", "tcga_laml.maf.gz", package = "maftools")
laml <- read_maf(maf = laml.maf)
if (require("BSgenome.Hsapiens.UCSC.hg19")) {
    mt_tally <- sig_tally(
        laml, 
```
### sig_unify_extract

An Unified Interface to Extract Signatures

**Description**

This function provides an unified interface to signature extractor implemented in `sigminer`. If you determine a specific approach, please also read the documentation of corresponding extractor. See "Arguments" part.

**Usage**

```r
sig_unify_extract(
  nmf_matrix,
  range = 2:5,
  nrun = 10,
  approach = c("bayes_nmf", "repeated_nmf", "bootstrap_nmf", "sigprofiler"),
  cores = 1L,
  ...
)
```

**Arguments**

- `nmf_matrix` a matrix used for NMF decomposition with rows indicate samples and columns indicate components.
- `range` signature number range, i.e. 2:5.
- `nrun` the number of iteration to be performed to extract each signature number.
- `approach` approach name.
  - "repeated_nmf" - `sig_extract`
simulated_catalogs

A List of Simulated SBS-96 Catalog Matrix

Description

Data from doi:10.1038/s4301802000275. 5 simulated mutation catalogs are used by the paper but only 4 are available. The data are simulated from COSMIC mutational signatures 1, 2, 3, 5, 6, 8, 12, 13, 17 and 18. Each sample is a linear combination of 5 randomly selected signatures with the addition of Poisson noise. The number of mutation in each sample is randomly selected between 1,000 and 50,000 mutations, in log scale so that a lower number of mutations is more likely to be selected. The proportion of each signature in each sample is also random.

Format

A list of matrix
**Source**

Generate from code under data_raw/

**Examples**

```r
data(simulated_catalogs)
```

---

**Simulation Analysis**

**Description**

- `simulate_signature()` - Simulate signatures from signature pool.
- `simulate_catalogue()` - Simulate catalogs from signature/catalog pool.
- `simulate_catalogue_matrix()` - Simulate a bootstrapped catalog matrix.

**Usage**

```r
simulate_signature(x, weights = NULL)
simulate_catalogue(x, n, weights = NULL)
simulate_catalogue_matrix(x)
```

**Arguments**

- **x**
  a numeric vector representing a signature/catalog or matrix with rows representing signatures/samples and columns representing components.
- **weights**
  a numeric vector for weights.
- **n**
  an integer indicating mutation number to be generated in a catalog.

**Value**

a matrix.

**Examples**

```r
# Generate a catalog
set.seed(1234)
catalog <- as.integer(table(sample(1:96, 1000, replace = TRUE)))
names(catalog) <- paste0("comp", 1:96)
# Generate a signature
sig <- catalog / sum(catalog)
# Simulate catalogs
x1 <- simulate_catalogue(catalog, 10) # 10 mutations
x1
```
```r
# Load SBS signature
load(system.file("extdata", "toy_mutational_signature.RData", package = "sigminer", mustWork = TRUE))
s <- t(sig2$Signature.norm)

# Generate a signature from multiple signatures/catalogs
s1 <- simulate_signature(s)
s1
s2 <- simulate_signature(s, weights = 1:3)
s2

# Generate a catalog from multiple signatures/catalogs
c1 <- simulate_catalogue(s, 100, weights = 1:3)
c1
```

---

**subset.CopyNumber**  
*Subsetting CopyNumber object*

**Description**

Subset data slot of `CopyNumber` object, un-selected rows will move to dropoff.segs slot, annotation slot will update in the same way.

**Usage**

```r
## S3 method for class 'CopyNumber'
subset(x, subset = TRUE, ...)
```

**Arguments**

- `x`  
  a `CopyNumber` object to be subsetted.

- `subset`  
  logical expression indicating rows to keep.

- `...`  
  further arguments to be passed to or from other methods. Useless here.

**Value**

a `CopyNumber` object

**Author(s)**

Shixiang Wang
### transcript.hg19

**Merged Transcript Location at Genome Build hg19**

**Description**

Merged Transcript Location at Genome Build hg19

**Format**

A data.table

**Source**

from GENCODE release v33.

**Examples**

```r
data(transcript.hg19)
```

### transcript.hg38

**Merged Transcript Location at Genome Build hg38**

**Description**

Merged Transcript Location at Genome Build hg38

**Format**

A data.table

**Source**

from GENCODE release v33.

**Examples**

```r
data(transcript.hg38)
```
### transcript.mm10

**Merged Transcript Location at Genome Build mm10**

**Description**

Merged Transcript Location at Genome Build mm10

**Format**

A `data.table`

**Source**

from GENCODE release M25.

**Examples**

```r
data(transcript.mm10)
```

---

### transcript.mm9

**Merged Transcript Location at Genome Build mm9**

**Description**

Merged Transcript Location at Genome Build mm9

**Format**

A `data.table`

**Source**

from UCSC [http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/transcriptome.txt.gz](http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/transcriptome.txt.gz)

**Examples**

```r
data(transcript.mm9)
```
transform_seg_table  

Transform Copy Number Table

Description

Transform Copy Number Table

Usage

transform_seg_table(
  data,
  genome_build = c("hg19", "hg38", "mm10", "mm9"),
  ref_type = c("cytoband", "gene"),
  values_fill = NA,
  values_fn = function(x, ...) {
    round(mean(x, ...))
  },
  resolution_factor = 1L
)

Arguments

data a CopyNumber object or a data.frame containing at least 'chromosome', 'start', 'end', 'segVal', 'sample' these columns.

genome_build genome build version, used when data is a data.frame, should be 'hg19' or 'hg38'.

ref_type annotation data type used for constructing matrix.

values_fill Optionally, a (scalar) value that specifies what each value should be filled in with when missing.

values_fn Optionally, a function applied to the value in each cell in the output. You will typically use this when the combination of id_cols and names_from columns does not uniquely identify an observation.

resolution_factor an integer to control the resolution. When it is 1 (default), compute frequency in each cytoband. When it is 2, use compute frequency in each half cytoband.

Value

a data.table.
Examples

load(system.file("extdata", "toy_copynumber.RData", 
    package = "sigminer", mustWork = TRUE
));
# Compute the mean segVal in each cytoband
x <- transform_seg_table(cn, resolution_factor = 1)
x
# Compute the mean segVal in each half-cytoband
x2 <- transform_seg_table(cn, resolution_factor = 2)
x2

use_color_style

Set Color Style for Plotting

Description

Set Color Style for Plotting

Usage

use_color_style(
    style, 
    mode = c("SBS", "copynumber", "DBS", "ID", "RS"), 
    method = "Wang"
)

Arguments

style one of 'default' and 'cosmic'.
mode only used when the style is 'cosmic', can be one of "SBS", "copynumber", "DBS", "ID".
method used to set a more custom palette for different methods.

Value

color values.

Examples

use_color_style("default")
use_color_style("cosmic")
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