

Package ‘decoupleR’

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Type Package

Title decoupleR: Ensemble of computational methods to infer biological activities from omics data

Version 2.2.2

Description Many methods allow us to extract biological activities from omics data using information from prior knowledge resources, reducing the dimensionality for increased statistical power and better interpretability. Here, we present decoupleR, a Bioconductor package containing different statistical methods to extract these signatures within a unified framework. decoupleR allows the user to flexibly test any method with any resource. It incorporates methods that take into account the sign and weight of network interactions. decoupleR can be used with any omic, as long as its features can be linked to a biological process based on prior knowledge. For example, in transcriptomics gene sets regulated by a transcription factor, or in phospho-proteomics phosphosites that are targeted by a kinase.

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URL <https://saezlab.github.io/decoupleR/>

BugReports <https://github.com/saezlab/decoupleR/issues>

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<code>.fit_preprocessing</code>	<i>Pre-processing for methods that fit networks.</i>
---------------------------------	--

Description

- If center is true, then the expression values are centered by the mean of expression across the samples.

Usage

```
.fit_preprocessing(network, mat, center, na.rm, sparse)
```

Arguments

<code>network</code>	Tibble or dataframe with edges and it's associated metadata.
<code>mat</code>	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
<code>center</code>	Logical value indicating if <code>mat</code> must be centered by <code>base::rowMeans()</code> .
<code>na.rm</code>	Should missing values (including NaN) be omitted from the calculations of <code>base::rowMeans()</code> ?
<code>sparse</code>	Deprecated parameter.

Value

A named list of matrices to evaluate in methods that fit models, like `.mlm_analysis()`.

- `mat`: Features as rows and samples as columns.
- `mor_mat`: Features as rows and columns as source.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))
net <- rename_net(net, source, target, mor)
.fit_preprocessing(net, mat, center = FALSE, na.rm = FALSE, sparse = FALSE)
```

check_corr	<i>Check correlation (colinearity)</i>
------------	--

Description

Checks the correlation across the regulators in a network.

Usage

```
check_corr(
  network,
  .source = "source",
  .target = "target",
  .mor = "mor",
  .likelihood = NULL
)
```

Arguments

network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.

Value

Correlation pairs tibble.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
net <- readRDS(file.path(inputs_dir, "net.rds"))
check_corr(net, .source='source')
```

convert_f_defaults	<i>Rename columns and add defaults values if column not present</i>
--------------------	---

Description

convert_f_defaults() combine the `dplyr::rename()` way of working and with the `tibble::add_column()` to add columns with default values in case they don't exist after renaming data.

Usage

```
convert_f_defaults(.data, ..., .def_col_val = c(), .use_dots = TRUE)
```

Arguments

<code>.data</code>	A data frame, data frame extension (e.g. a tibble), or a lazy data frame (e.g. from dbplyr or dtplyr). See <i>Methods</i> , below, for more details.
<code>...</code>	For <code>rename()</code> : <tidy-select> Use <code>new_name = old_name</code> to rename selected variables. For <code>rename_with()</code> : additional arguments passed onto <code>.fn</code> .
<code>.def_col_val</code>	Named vector with columns with default values if none exist after rename.
<code>.use_dots</code>	Should a dot prefix be added to renamed variables? This will allow swapping of columns.

Details

The objective of using `.use_dots` is to be able to swap columns which, by default, is not allowed by the `dplyr::rename()` function. The same behavior can be replicated by simply using the `dplyr::select()`, however, the `select` evaluation allows much more flexibility so that unexpected results could be obtained. Despite this, a future implementation will consider this form of execution to allow renaming the same column to multiple ones (i.e. extend dataframe extension).

Value

An object of the same type as `.data`. The output has the following properties:

- Rows are not affected.
- Column names are changed.
- Column order is the same as that of the function call.

Examples

```
df <- tibble::tibble(x = 1, y = 2, z = 3)

# Rename columns
df <- tibble::tibble(x = 1, y = 2)
convert_f_defaults(
  .data = df,
  new_x = x,
  new_y = y,
  new_z = NULL,
  .def_col_val = c(new_z = 3)
)
```

decouple

*Evaluate multiple statistics with same input data***Description**

Calculate the source activity per sample out of a gene expression matrix by coupling a regulatory network with a variety of statistics.

Usage

```
decouple(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  statistics = NULL,
  args = list(NULL),
  consensus_score = TRUE,
  consensus_stats = NULL,
  include_time = FALSE,
  show_toy_call = FALSE,
  minsize = 5
)
```

Arguments

<code>mat</code>	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
<code>network</code>	Tibble or dataframe with edges and it's associated metadata.
<code>.source</code>	Column with source nodes.
<code>.target</code>	Column with target nodes.
<code>statistics</code>	Statistical methods to be run sequentially. If none are provided, only top performer methods are run (mlm, ulm and wsum).
<code>args</code>	A list of argument-lists the same length as <code>statistics</code> (or length 1). The default argument, <code>list(NULL)</code> , will be recycled to the same length as <code>statistics</code> , and will call each function with no arguments (apart from <code>mat</code> , <code>network</code> , <code>.source</code> and <code>.target</code>).
<code>consensus_score</code>	Boolean whether to run a consensus score between methods.
<code>consensus_stats</code>	List of estimate names to use for the calculation of the consensus score. This is used to filter out extra estimations from some methods, for example <code>wsum</code> returns <code>wsum</code> , <code>corr_wsum</code> and <code>norm_wsum</code> . If none are provided, and also no statistics were provided, only top performer methods are used (mlm, ulm and <code>norm_wsum</code>). Else, it will use all available estimates after running all methods in the <code>statistics</code> argument.

<code>include_time</code>	Should the time per statistic evaluated be informed?
<code>show_toy_call</code>	The call of each statistic must be informed?
<code>minsize</code>	Integer indicating the minimum number of targets per source.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `run_id`: Indicates the order in which the methods have been executed.
2. `statistic`: Indicates which method is associated with which score.
3. `source`: Source nodes of network.
4. `condition`: Condition representing each column of `mat`.
5. `score`: Regulatory activity (enrichment score).
6. `statistic_time`: If requested, internal execution time indicator.
7. `p_value`: p-value (if available) of the obtained score.

See Also

Other `decoupleR` statistics: [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_gsva\(\)](#), [run_mdt\(\)](#), [run_mlm\(\)](#), [run_ora\(\)](#), [run_udt\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wmean\(\)](#), [run_wsum\(\)](#)

Examples

```
if (FALSE) {
  inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

  mat <- readRDS(file.path(inputs_dir, "mat.rds"))
  net <- readRDS(file.path(inputs_dir, "net.rds"))

  decouple(
    mat = mat,
    network = net,
    .source = "source",
    .target = "target",
    statistics = c("gsva", "wmean", "wsum", "ulm", "aucell"),
    args = list(
      gsva = list(verbose = FALSE),
      wmean = list(.mor = "mor", .likelihood = "likelihood"),
      wsum = list(.mor = "mor"),
      ulm = list(.mor = "mor")
    ),
    minsize = 0
  )
}
```

extract_sets	<i>Extract sets</i>
--------------	---------------------

Description

Extracts feature sets from a renamed network (see [rename_net](#)).

Usage

```
extract_sets(network)
```

Arguments

network Tibble or dataframe with edges and it's associated metadata.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))
net <- rename_net(net, source, target, mor)
extract_sets(net)
```

filt_minsize	<i>Filter sources with minsize targets</i>
--------------	--

Description

Filter sources of a net with less than minsize targets

Usage

```
filt_minsize(mat_f_names, network, minsize = 5)
```

Arguments

mat_f_names Feature names of mat.
network Tibble or dataframe with edges and it's associated metadata.
minsize Integer indicating the minimum number of targets per source.

Value

Filtered network.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))
net <- rename_net(net, source, target, mor)
filt_minsize(rownames(mat), net, minsize = 4)
```

get_dorothea

DoRothEA gene regulatory network.

Description

Wrapper to access DoRothEA gene regulatory network. DoRothEA is a comprehensive resource containing a curated collection of transcription factors (TFs) and their target genes. Each interaction is weighted by its mode of regulation (either positive or negative) and by its confidence level

Usage

```
get_dorothea(
  organism = "human",
  levels = c("A", "B", "C"),
  weight_dict = list(A = 1, B = 2, C = 3, D = 4)
)
```

Arguments

organism	Which organism to use. Only human and mouse are available.
levels	List of confidence levels to return. Goes from A to D, A being the most confident and D being the less.
weight_dict	Dictionary of values to divide the mode of regulation (-1 or 1), one for each confidence level. Bigger values will generate weights close to zero.

Examples

```
dorothea <- get_dorothea(organism='human', levels=c('A', 'B', 'C'))
```

get_progeny	<i>Pathway RespOnsive GENes for activity inference (PROGENy).</i>
-------------	---

Description

Wrapper to access PROGENy model gene weights. Each pathway is defined with a collection of target genes, each interaction has an associated p-value and weight. The top significant interactions per pathway are returned.

Usage

```
get_progeny(organism = "human", top = 500)
```

Arguments

organism	Which organism to use. Only human and mouse are available.
top	Number of genes per pathway to return.

Examples

```
progeny <- get_progeny(organism='human', top=500)
```

get_resource	<i>Wrapper to access resources inside Omnipath. This wrapper allows to easily query different prior knowledge resources. To check available resources run decoupleR::show_resources(). For more information visit the official website for Rhrefhttps://omnipathdb.org/Omnipath.</i>
--------------	--

Description

Wrapper to access resources inside Omnipath. This wrapper allows to easily query different prior knowledge resources. To check available resources run `decoupleR::show_resources()`. For more information visit the official website for [Omnipath](https://omnipathdb.org/Omnipath).

Usage

```
get_resource(name)
```

Arguments

name	Name of the resource to query.
------	--------------------------------

Examples

```
df <- decoupleR::get_resource('SIGNOR')
```

get_toy_data	<i>Generate a toy mat and network.</i>
--------------	--

Description

Generate a toy mat and network.

Usage

```
get_toy_data(n_samples = 24, seed = 42)
```

Arguments

n_samples	Number of samples to simulate.
seed	A single value, interpreted as an integer, or NULL for random number generation.

Value

List containing mat and network.

Examples

```
data <- get_toy_data()
mat <- data$mat
network <- data$network
```

intersect_regulons	<i>Intersect network target features with input matrix.</i>
--------------------	---

Description

Keep only edges which its target features belong to the input matrix.

Usage

```
intersect_regulons(mat, network, .source, .target, minsize)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. rownames(mat) must have at least one intersection with the elements in network .target column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
minsize	Minimum number of targets per source allowed.

Value

Filtered tibble.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))
intersect_regulons(mat, net, source, target, minsize=4)
```

rename_net

Rename network

Description

Renames a given network to these column names: .source, .target, .mor. If .mor is not provided, then the function sets them to default values.

Usage

```
rename_net(
  network,
  .source,
  .target,
  .mor = NULL,
  .likelihood = NULL,
  def_mor = 1
)
```

Arguments

network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
def_mor	Default value for .mor when not provided.

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))
rename_net(net, source, target, mor)
```

run_aucell	<i>AUCell</i>
------------	---------------

Description

Calculates regulatory activities using AUCCell.

Usage

```
run_aucell(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  aucMaxRank = ceiling(0.05 * nrow(rankings)),
  nproc = 4,
  seed = 42,
  minsize = 5
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network .target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
aucMaxRank	Threshold to calculate the AUC.
nproc	Number of cores to use for computation.
seed	A single value, interpreted as an integer, or NULL for random number generation.
minsize	Integer indicating the minimum number of targets per source.

Details

AUCCell (Aibar et al., 2017) uses the Area Under the Curve (AUC) to calculate whether a set of targets is enriched within the molecular readouts of each sample. To do so, AUCCell first ranks the molecular features of each sample from highest to lowest value, resolving ties randomly. Then, an AUC can be calculated using by default the top 5% molecular features in the ranking. Therefore, this metric, `aucell`, represents the proportion of abundant molecular features in the target set, and their relative abundance value compared to the other features within the sample.

Aibar S. et al. (2017) Scenic: single-cell regulatory network inference and clustering. *Nat. Methods*, 14, 1083–1086.

See Also

Other decoupleR statistics: `decouple()`, `run_fgsea()`, `run_gsva()`, `run_mdt()`, `run_mlm()`, `run_ora()`, `run_udt()`, `run_ulm()`, `run_viper()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_aucell(mat, net, minsize=0, nproc=1, aucMaxRank=3)
```

run_consensus

Consensus score between methods

Description

Function to generate a consensus score between methods from the result of the decouple function.

Usage

```
run_consensus(df, include_time = FALSE, seed = NULL)
```

Arguments

<code>df</code>	decouple data frame result
<code>include_time</code>	Should the time per statistic evaluated be informed?
<code>seed</code>	Deprecated parameter.

Value

Updated tibble with the computed consensus score between methods

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

results <- decouple(
  mat = mat,
  network = net,
  .source = "source",
  .target = "target",
  statistics = c("wmean", "ulm"),
  args = list(
    wmean = list(.mor = "mor", .likelihood = "likelihood"),
```

```

        ulm = list(.mor = "mor", .likelihood = "likelihood")
      ),
      consensus_score = FALSE,
      minsize = 0
    )
  run_consensus(results)

```

run_fgsea

*Fast Gene Set Enrichment Analysis (FGSEA)***Description**

Calculates regulatory activities using FGSEA.

Usage

```

run_fgsea(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  times = 100,
  nproc = 4,
  seed = 42,
  minsize = 5,
  ...
)

```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
times	How many permutations to do?
nproc	Number of cores to use for computation.
seed	A single value, interpreted as an integer, or NULL.
minsize	Integer indicating the minimum number of targets per source.
...	Arguments passed on to <code>fgsea::fgseaMultilevel</code>
sampleSize	The size of a random set of genes which in turn has size = <code>pathwaySize</code>
minSize	Minimal size of a gene set to test. All pathways below the threshold are excluded.

`maxSize` Maximal size of a gene set to test. All pathways above the threshold are excluded.

`eps` This parameter sets the boundary for calculating the p value.

`scoreType` This parameter defines the GSEA score type. Possible options are ("std", "pos", "neg")

`gseaParam` GSEA parameter value, all gene-level statis are raised to the power of 'gseaParam' before calculation of GSEA enrichment scores.

`BPPARAM` Parallelization parameter used in `bplapply`. Can be used to specify cluster to run. If not initialized explicitly or by setting 'nproc' default value 'bpparam()' is used.

`absEps` deprecated, use 'eps' parameter instead

Details

GSEA (Aravind et al., 2005) starts by transforming the input molecular readouts in `mat` to ranks for each sample. Then, an enrichment score `fgsea` is calculated by walking down the list of features, increasing a running-sum statistic when a feature in the target feature set is encountered and decreasing it when it is not. The final score is the maximum deviation from zero encountered in the random walk. Finally, a normalized score `norm_fgsea`, can be obtained by computing the z-score of the estimate compared to a null distribution obtained from `N` random permutations. The used implementation is taken from the package `fgsea` (Korotkevich et al., 2021).

Aravind S. et al. (2005) Gene set enrichment analysis: A knowledge-based approach for interpreting genome-wide expression profiles. *PNAS*. 102, 43.

Korotkevich G. et al. (2021) Fast gene set enrichment analysis. *bioRxiv*. DOI: <https://doi.org/10.1101/060012>.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other `decoupleR` statistics: `decouple()`, `run_aucell()`, `run_gsva()`, `run_mdt()`, `run_mlm()`, `run_ora()`, `run_udt()`, `run_ulm()`, `run_viper()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_fgsea(mat, net, minsize=0, nproc=1)
```

`run_gsva`*Gene Set Variation Analysis (GSVA)*

Description

Calculates regulatory activities using GSVA.

Usage

```
run_gsva(  
  mat,  
  network,  
  .source = .data$source,  
  .target = .data$target,  
  verbose = FALSE,  
  method = "gsva",  
  minsize = 5,  
  ...  
)
```

Arguments

<code>mat</code>	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
<code>network</code>	Tibble or dataframe with edges and it's associated metadata.
<code>.source</code>	Column with source nodes.
<code>.target</code>	Column with target nodes.
<code>verbose</code>	Gives information about each calculation step. Default: FALSE.
<code>method</code>	Method to employ in the estimation of gene-set enrichment. scores per sample. By default this is set to <code>gsva</code> (Hänzelmann et al, 2013).
<code>minsize</code>	Integer indicating the minimum number of targets per source.
<code>...</code>	Arguments passed on to GSVA::gsva

Details

GSVA (Hänzelmann et al., 2013) starts by transforming the input molecular readouts in `mat` to a readout-level statistic using Gaussian kernel estimation of the cumulative density function. Then, readout-level statistics are ranked per sample and normalized to up-weight the two tails of the rank distribution. Afterwards, an enrichment score `gsva` is calculated using a running sum statistic that is normalized by subtracting the largest negative estimate from the largest positive one.

Hänzelmann S. et al. (2013) GSVA: gene set variation analysis for microarray and RNA-seq data. BMC Bioinformatics, 14, 7.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other decoupleR statistics: [decouple\(\)](#), [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_mdt\(\)](#), [run_mlm\(\)](#), [run_ora\(\)](#), [run_udt\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wmean\(\)](#), [run_wsum\(\)](#)

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_gsva(mat, net, minsize=0, verbose = FALSE)
```

`run_mdt`*Multivariate Decision Trees (MDT)*

Description

Calculates regulatory activities using MDT.

Usage

```
run_mdt(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  sparse = FALSE,
  center = FALSE,
  na.rm = FALSE,
  trees = 10,
  min_n = 20,
  nproc = 4,
  seed = 42,
  minsize = 5
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
sparse	Deprecated parameter.
center	Logical value indicating if <code>mat</code> must be centered by <code>base::rowMeans()</code> .
na.rm	Should missing values (including NaN) be omitted from the calculations of <code>base::rowMeans()</code> ?
trees	An integer for the number of trees contained in the ensemble.
min_n	An integer for the minimum number of data points in a node that are required for the node to be split further.
nproc	Number of cores to use for computation.
seed	A single value, interpreted as an integer, or NULL for random number generation.
minsize	Integer indicating the minimum number of targets per source.

Details

MDT fits a multivariate regression random forest for each sample, where the observed molecular readouts in `mat` are the response variable and the regulator weights in `net` are the covariates. Target features with no associated weight are set to zero. The obtained feature importances from the fitted model are the activities `mdt` of the regulators in `net`.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other decoupleR statistics: `decouple()`, `run_aucell()`, `run_fgsea()`, `run_gsva()`, `run_mlm()`, `run_ora()`, `run_udt()`, `run_ulm()`, `run_viper()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_mdt(mat, net, minsize=0)
```

run_mlm

*Multivariate Linear Model (MLM)***Description**

Calculates regulatory activities using MLM.

Usage

```
run_mlm(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  sparse = FALSE,
  center = FALSE,
  na.rm = FALSE,
  minsize = 5
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
sparse	Deprecated parameter.
center	Logical value indicating if <code>mat</code> must be centered by <code>base::rowMeans()</code> .
na.rm	Should missing values (including NaN) be omitted from the calculations of <code>base::rowMeans()</code> ?
minsize	Integer indicating the minimum number of targets per source.

Details

MLM fits a multivariate linear model for each sample, where the observed molecular readouts in `mat` are the response variable and the regulator weights in `net` are the covariates. Target features with no associated weight are set to zero. The obtained t-values from the fitted model are the activities (`mlm`) of the regulators in `net`.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other `decoupleR` statistics: [decouple\(\)](#), [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_gsva\(\)](#), [run_mdt\(\)](#), [run_ora\(\)](#), [run_udt\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wmean\(\)](#), [run_wsum\(\)](#)

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_mlm(mat, net, minsize=0)
```

run_ora

Over Representation Analysis (ORA)

Description

Calculates regulatory activities using ORA.

Usage

```
run_ora(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  n_up = ceiling(0.05 * nrow(mat)),
  n_bottom = 0,
  n_background = 20000,
```

```

with_ties = TRUE,
seed = 42,
minsize = 5,
...
)

```

Arguments

<code>mat</code>	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
<code>network</code>	Tibble or dataframe with edges and it's associated metadata.
<code>.source</code>	Column with source nodes.
<code>.target</code>	Column with target nodes.
<code>n_up</code>	Integer indicating the number of top targets to slice from <code>mat</code> .
<code>n_bottom</code>	Integer indicating the number of bottom targets to slice from <code>mat</code> .
<code>n_background</code>	Integer indicating the background size of the sliced targets. If not specified the number of background targets is determined by the total number of unique targets in the union of <code>mat</code> and <code>network</code> .
<code>with_ties</code>	Should ties be kept together? The default, <code>TRUE</code> , may return more rows than you request. Use <code>FALSE</code> to ignore ties, and return the first <code>n</code> rows.
<code>seed</code>	A single value, interpreted as an integer, or <code>NULL</code> for random number generation.
<code>minsize</code>	Integer indicating the minimum number of targets per source.
<code>...</code>	Arguments passed on to <code>stats::fisher.test</code>
<code>workspace</code>	an integer specifying the size of the workspace used in the network algorithm. In units of 4 bytes. Only used for non-simulated p-values larger than 2×2 tables. Since R version 3.5.0, this also increases the internal stack size which allows larger problems to be solved, however sometimes needing hours. In such cases, <code>simulate.p.values=TRUE</code> may be more reasonable.
<code>hybrid</code>	a logical. Only used for larger than 2×2 tables, in which cases it indicates whether the exact probabilities (default) or a hybrid approximation thereof should be computed.
<code>hybridPars</code>	a numeric vector of length 3, by default describing ‘‘Cochran’s conditions’’ for the validity of the chisquare approximation, see ‘Details’.
<code>control</code>	a list with named components for low level algorithm control. At present the only one used is <code>"mult"</code> , a positive integer ≥ 2 with default 30 used only for larger than 2×2 tables. This says how many times as much space should be allocated to paths as to keys: see file ‘ <code>fexact.c</code> ’ in the sources of this package.
<code>or</code>	the hypothesized odds ratio. Only used in the 2×2 case.
<code>alternative</code>	indicates the alternative hypothesis and must be one of <code>"two.sided"</code> , <code>"greater"</code> or <code>"less"</code> . You can specify just the initial letter. Only used in the 2×2 case.

- `conf.int` logical indicating if a confidence interval for the odds ratio in a 2×2 table should be computed (and returned).
- `conf.level` confidence level for the returned confidence interval. Only used in the 2×2 case and if `conf.int = TRUE`.
- `simulate.p.value` a logical indicating whether to compute p-values by Monte Carlo simulation, in larger than 2×2 tables.
- `B` an integer specifying the number of replicates used in the Monte Carlo test.

Details

ORA measures the overlap between the target feature set and a list of most altered molecular features in `mat`. The most altered molecular features can be selected from the top and or bottom of the molecular readout distribution, by default it is the top 5% positive values. With these, a contingency table is build and a one-tailed Fisher's exact test is computed to determine if a regulator's set of features are over-represented in the selected features from the data. The resulting score, `ora`, is the minus log10 of the obtained p-value.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other decoupleR statistics: `decouple()`, `run_aucell()`, `run_fgsea()`, `run_gsva()`, `run_mdt()`, `run_mlm()`, `run_udt()`, `run_ulm()`, `run_viper()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_ora(mat, net, minsize=0)
```

run_udt *Univariate Decision Tree (UDT)*

Description

Calculates regulatory activities by using UDT.

Usage

```
run_udt(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  sparse = FALSE,
  center = FALSE,
  na.rm = FALSE,
  min_n = 20,
  seed = 42,
  minsize = 5
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
sparse	Deprecated parameter.
center	Logical value indicating if <code>mat</code> must be centered by <code>base::rowMeans()</code> .
na.rm	Should missing values (including NaN) be omitted from the calculations of <code>base::rowMeans()</code> ?
min_n	An integer for the minimum number of data points in a node that are required for the node to be split further.
seed	A single value, interpreted as an integer, or NULL for random number generation.
minsize	Integer indicating the minimum number of targets per source.

Details

UDT fits a single regression decision tree for each sample and regulator, where the observed molecular readouts in `mat` are the response variable and the regulator weights in `net` are the explanatory one. Target features with no associated weight are set to zero. The obtained feature importance from the fitted model is the activity `udt` of a given regulator.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other `decoupleR` statistics: [decouple\(\)](#), [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_gsva\(\)](#), [run_mdt\(\)](#), [run_mlm\(\)](#), [run_ora\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wmean\(\)](#), [run_wsum\(\)](#)

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_udt(mat, net, minsize=0)
```

run_ulm

Univariate Linear Model (ULM)

Description

Calculates regulatory activities using ULM.

Usage

```
run_ulm(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  sparse = FALSE,
```

```

center = FALSE,
na.rm = FALSE,
minsize = 5
)

```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
sparse	Deprecated parameter.
center	Logical value indicating if <code>mat</code> must be centered by <code>base::rowMeans()</code> .
na.rm	Should missing values (including NaN) be omitted from the calculations of <code>base::rowMeans()</code> ?
minsize	Integer indicating the minimum number of targets per source.

Details

ULM fits a linear model for each sample and regulator, where the observed molecular readouts in `mat` are the response variable and the regulator weights in `net` are the explanatory one. Target features with no associated weight are set to zero. The obtained t-value from the fitted model is the activity `ulm` of a given regulator.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other decoupleR statistics: `decouple()`, `run_aucell()`, `run_fgsea()`, `run_gsva()`, `run_mdt()`, `run_mlm()`, `run_ora()`, `run_udt()`, `run_viper()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_ulm(mat, net, minsize=0)
```

run_viper	<i>Virtual Inference of Protein-activity by Enriched Regulon analysis (VIPER)</i>
-----------	---

Description

Calculates regulatory activities using VIPER.

Usage

```
run_viper(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  verbose = FALSE,
  minsize = 5,
  pleiotropy = TRUE,
  eset.filter = FALSE,
  ...
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network .target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
verbose	Logical, whether progression messages should be printed in the terminal.
minsize	Integer indicating the minimum number of targets per source.
pleiotropy	Logical, whether correction for pleiotropic regulation should be performed.

<code>eset.filter</code>	Logical, whether the dataset should be limited only to the genes represented in the interactome.
<code>...</code>	Arguments passed on to <code>viper::viper</code>
<code>dnull</code>	Numeric matrix for the null model, usually generated by <code>nullTtest</code>
<code>nes</code>	Logical, whether the enrichment score reported should be normalized
<code>method</code>	Character string indicating the method for computing the single samples signature, either <code>scale</code> , <code>rank</code> , <code>mad</code> , <code>ttest</code> or <code>none</code>
<code>bootstraps</code>	Integer indicating the number of bootstraps iterations to perform. Only the <code>scale</code> method is implemented with bootstraps.
<code>adaptive.size</code>	Logical, whether the weighting scores should be taken into account for computing the regulon size
<code>pleiotropyArgs</code>	list of 5 numbers for the pleiotropy correction indicating: regulators p-value threshold, pleiotropic interaction p-value threshold, minimum number of targets in the overlap between pleiotropic regulators, penalty for the pleiotropic interactions and the method for computing the pleiotropy, either <code>absolute</code> or <code>adaptive</code>
<code>cores</code>	Integer indicating the number of cores to use (only 1 in Windows-based systems)

Details

VIPER (Alvarez et al., 2016) estimates biological activities by performing a three-tailed enrichment score calculation. For further information check the supplementary information of the decoupleR manuscript or the original publication.

Alvarez M.J. et al. (2016) Functional characterization of somatic mutations in cancer using network-based inference of protein activity. *Nat. Genet.*, 48, 838–847.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).

See Also

Other decoupleR statistics: `decouple()`, `run_aucell()`, `run_fgsea()`, `run_gsva()`, `run_mdt()`, `run_mlm()`, `run_ora()`, `run_udt()`, `run_ulm()`, `run_wmean()`, `run_wsum()`

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")
mat <- readRDS(file.path(inputs_dir, "mat.rds"))
```

```
net <- readRDS(file.path(inputs_dir, "net.rds"))
run_viper(mat, net, minsize=0, verbose = FALSE)
```

run_wmean	<i>Weighted Mean (WMEAN)</i>
-----------	------------------------------

Description

Calculates regulatory activities using WMEAN.

Usage

```
run_wmean(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
  .likelihood = .data$likelihood,
  times = 100,
  seed = 42,
  sparse = TRUE,
  randomize_type = "rows",
  minsize = 5
)
```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. <code>rownames(mat)</code> must have at least one intersection with the elements in <code>network</code> <code>.target</code> column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
times	How many permutations to do?
seed	A single value, interpreted as an integer, or NULL for random number generation.
sparse	Should the matrices used for the calculation be sparse?
randomize_type	How to randomize the expression matrix.
minsize	Integer indicating the minimum number of targets per source.

Details

WMEAN infers regulator activities by first multiplying each target feature by its associated weight which then are summed to an enrichment score `wmean`. Furthermore, permutations of random target features can be performed to obtain a null distribution that can be used to compute a z-score `norm_wmean`, or a corrected estimate `corr_wmean` by multiplying `wmean` by the minus log10 of the obtained empirical p-value.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. `statistic`: Indicates which method is associated with which score.
2. `source`: Source nodes of network.
3. `condition`: Condition representing each column of `mat`.
4. `score`: Regulatory activity (enrichment score).
5. `p_value`: p-value for the score of the method.

See Also

Other decoupleR statistics: [decouple\(\)](#), [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_gsva\(\)](#), [run_mdt\(\)](#), [run_mlm\(\)](#), [run_ora\(\)](#), [run_udt\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wsum\(\)](#)

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_wmean(mat, net, minsize=0)
```

run_wsum

Weighted Sum (WSUM)

Description

Calculates regulatory activities using WSUM.

Usage

```
run_wsum(
  mat,
  network,
  .source = .data$source,
  .target = .data$target,
  .mor = .data$mor,
```

```

    .likelihood = .data$likelihood,
    times = 100,
    seed = 42,
    sparse = TRUE,
    randomize_type = "rows",
    minsize = 5
  )

```

Arguments

mat	Matrix to evaluate (e.g. expression matrix). Target nodes in rows and conditions in columns. rownames(mat) must have at least one intersection with the elements in network .target column.
network	Tibble or dataframe with edges and it's associated metadata.
.source	Column with source nodes.
.target	Column with target nodes.
.mor	Column with edge mode of regulation (i.e. mor).
.likelihood	Deprecated argument. Now it will always be set to 1.
times	How many permutations to do?
seed	A single value, interpreted as an integer, or NULL for random number generation.
sparse	Should the matrices used for the calculation be sparse?
randomize_type	How to randomize the expression matrix.
minsize	Integer indicating the minimum number of targets per source.

Details

WSUM infers regulator activities by first multiplying each target feature by its associated weight which then are summed to an enrichment score wsum. Furthermore, permutations of random target features can be performed to obtain a null distribution that can be used to compute a z-score norm_wsum, or a corrected estimate corr_wsum by multiplying wsum by the minus log10 of the obtained empirical p-value.

Value

A long format tibble of the enrichment scores for each source across the samples. Resulting tibble contains the following columns:

1. statistic: Indicates which method is associated with which score.
2. source: Source nodes of network.
3. condition: Condition representing each column of mat.
4. score: Regulatory activity (enrichment score).
5. p_value: p-value for the score of the method.

See Also

Other decoupleR statistics: [decouple\(\)](#), [run_aucell\(\)](#), [run_fgsea\(\)](#), [run_gsva\(\)](#), [run_mdt\(\)](#), [run_mlm\(\)](#), [run_ora\(\)](#), [run_udt\(\)](#), [run_ulm\(\)](#), [run_viper\(\)](#), [run_wmean\(\)](#)

Examples

```
inputs_dir <- system.file("testdata", "inputs", package = "decoupleR")

mat <- readRDS(file.path(inputs_dir, "mat.rds"))
net <- readRDS(file.path(inputs_dir, "net.rds"))

run_wsum(mat, net, minsize=0)
```

show_methods	<i>Show methods</i>
--------------	---------------------

Description

Prints the methods available in decoupleR. The first column correspond to the function name in decoupleR and the second to the method's full name.

Usage

```
show_methods()
```

Examples

```
show_methods()
```

show_resources	<i>Shows available resources in Omnipath. For more information visit the official website for Rhrefhttps://omnipathdb.org/Omnipath.</i>
----------------	---

Description

Shows available resources in Omnipath. For more information visit the official website for **Omni-path**.

Usage

```
show_resources()
```

Examples

```
decoupleR::show_resources()
```


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