Package 'cosmosR'

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Type Package

Title COSMOS (Causal Oriented Search of Multi-Omic Space)

Version 1.2.0

Description COSMOS (Causal Oriented Search of Multi-Omic Space) is a method that integrates phosphoproteomics, transcriptomics, and metabolomics data sets based on prior knowledge of signaling, metabolic, and gene regulatory networks. It estimated the activities of transcrption factors and kinases and finds a network-level causal reasoning. Thereby, COSMOS provides mechanistic hypotheses for experimental observations across mulit-omics datasets.

URL https://github.com/saezlab/COSMOSR

BugReports https://github.com/saezlab/COSMOSR/issues

Depends R (>= 4.1)

License GPL-3

Encoding UTF-8

LazyData false

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Imports AnnotationDbi, biomaRt, CARNIVAL, dorothea, dplyr, ggplot2, GSEABase, igraph, magrittr, org.Hs.eg.db, plyr, purrr, readr, rlang, scales, stringr, tibble, utils, visNetwork

Suggests testthat, knitr, rmarkdown, piano

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R topics documented:

`convert_ensembl_to_entrezid` *convert gene ensembl to entrez id*

Description

convert gene ensembl to entrez id

Usage

```
convert_ensembl_to_entrezid(ensembl)
```

Arguments

ensembl	vector of genes with ensembl id

Value

named vector, where names are the old ensemblIDs and values are the entrezIDs

See Also

convert_genesymbols_to_entrezid

Examples

```
ensembl <- c("ENSG00000100601", "ENSG00000178826", "ENSG00000138231")
entrez_map <- convert_ensembl_to_entrezid(ensembl)
```

---

convert_genesymbols_to_entrezid

convert gene symbols to entrez id

Description

convert gene symbols to entrez id

Usage

```
convert_genesymbols_to_entrezid(symbols)
```

Arguments

symbols	vector of genesymbols

Value

data.frame with human gene ENTREZID and SYMBOL mapping

See Also

convert_ensembl_to_entrezid

Examples

```
symbols <- c("MDH1", "PARP1", "IL6")
symbol_entrez_map <- convert_genesymbols_to_entrezid(symbols)
```

cosmos_data *Create Cosmos Data*

Description

An S3 class that combines the required data into a comprehensive list. Use the preprocess_COSMOS_signaling_to_metabol or preprocess_COSMOS_metabolism_to_signaling to create an instance.

Usage

```
cosmos_data(
  meta_network,
  tf_regulon = NULL,
  signaling_data,
  metabolic_data,
  expression_data,
  verbose = TRUE
)
```

Arguments

meta_network	Prior knowledge network (PKN). By default COSMOS use a PKN derived from Omnipath, STITCHdb and Recon3D. See details on the data meta_network.
tf_regulon	Collection of transcription factor - target interactions. A default collection from dorothea can be obtained by the load_tf_regulon_dorothea function.
signaling_data	Numerical vector, where names are signaling nodes in the PKN and values are from {1, 0, -1}. Continuous data will be discretized using the sign function.
metabolic_data	Numerical vector, where names are metabolic nodes in the PKN and values are continuous values that represents log2 fold change or t-values from a differential analysis. These values are compared to the simulation results (simulated nodes can take value -1, 0 or 1).
expression_data	Numerical vector that represents the results of a differential gene expression analysis. Names are gene names using EntrezID starting with an X and values are log fold change or t-values. Genes with NA values are considered none expressed and they will be removed from the TF-gene expression interactions.
verbose	(default: TRUE) Reports details about the cosmos_data object.

Value

cosmos data class instance.

default_CARNIVAL_options *Setting Default CARNIVAL Options*

Description

Returns the default CARNIVAL options as a list. You can modify the elements of the list and then use it as an argument in "run_COSMOS()".

Usage

```
default_CARNIVAL_options()
```

Value

returns a list with all possible options implemented in CARNIVAL. see the documentation on runCARNIVAL.

Examples

```
# load and change default options:
my_options = default_CARNIVAL_options()

my_options$solverPath = "/Applications/CPLEX_Studio128/cplex/bin/x86-64_osx/cplex"
my_options$threads = 2
my_options$timelimit = 3600*15
```

display_node_neighboorhood *display_node_neighboorhood*

Description

display input and measurements within n steps of a given set of nodes

Usage

```
display_node_neighboorhood(central_node, sif, att, n = 100)
```

Arguments

central_node	character or character vector; node ID(s) around which a network will be branched out untill meansurments and input are reached
sif	df; COSMOS network solution in sif format like the first list element returned by the format_cosmos_res function
att	df; attributes of the nodes of the COMSOS network solution like the second list element returned by the format_cosmos_res function
n	numeric; maximum number of steps in the network to look for inputs and measurments

Value

a visnetwork object

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_for <- preprocess_COSMOS_signaling_to_metabolism(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
test_result_for <- run_COSMOS_signaling_to_metabolism(data = test_for,
CARNIVAL_options = CARNIVAL_options)
data(metabolite_to_pubchem)
data(omnipath_ptm)
test_result_for <- format_COSMOS_res(test_result_for,
metab_mapping = metabolite_to_pubchem,
measured_nodes = unique(c(names(toy_metabolic_input),
                          names(toy_signaling_input))),
omnipath_ptm = omnipath_ptm)
network_plot <- display_node_neighboorhood(central_node = 'NFKB1',
sif = test_result_for[[1]],
att = test_result_for[[2]],
n = 7)
network_plot
```

`extract_nodes_for_ORA` *Extract COSMOS nodes for ORA analysis*

Description

Function to extract the nodes that appear in the COSMOS output network and the background genes (all genes present in the prior knowledge network)

Usage

```
extract_nodes_for_ORA(sif, att)
```

Arguments

`sif`	df; COSMOS network solution in sif format like the first list element returned by the format_cosmos_res function
`att`	df; attributes of the nodes of the COMSOS network solution like the second list element returned by the format_cosmos_res function

Value

List with 2 objects: the success and the background genes

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_for <- preprocess_COSMOS_signaling_to_metabolism(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
test_result_for <- run_COSMOS_signaling_to_metabolism(data = test_for,
CARNIVAL_options = CARNIVAL_options)
data(metabolite_to_pubchem)
data(omnipath_ptm)
test_result_for <- format_COSMOS_res(test_result_for,
metab_mapping = metabolite_to_pubchem,
measured_nodes = unique(c(names(toy_metabolic_input),
                          names(toy_signaling_input))),
omnipath_ptm = omnipath_ptm)
extreacted_nodes <- extract_nodes_for_ORA(
```

```
sif = test_result_for[[1]],
att = test_result_for[[2]]
)
```

`format_COSMOS_res` *format_COSMOS_res*

Description

formats the network with readable names

Usage

```
format_COSMOS_res(
  cosmos_res,
  metab_mapping,
  gene_mapping = "org.Hs.eg.db",
  measured_nodes,
  omnipath_ptm
)
```

Arguments

`cosmos_res`	results of CARNIVAL run
`metab_mapping`	a named vector with pubchem cid as names and desired metabolite names as values.
`gene_mapping`	by default, use the 'org.Hs.eg.db' to map gene names. Can also be a named vector with entrez gene id as names and desired gene names as values.
`measured_nodes`	vector of nodes that are measured or inputs
`omnipath_ptm`	ptms database from OmnipathR

Value

list with network and attribute tables.

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_for <- preprocess_COSMOS_signaling_to_metabolism(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
```

```
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
test_result_for <- run_COSMOS_signaling_to_metabolism(data = test_for,
CARNIVAL_options = CARNIVAL_options)
data(metabolite_to_pubchem)
data(omnipath_ptm)
test_result_for <- format_COSMOS_res(test_result_for,
metab_mapping = metabolite_to_pubchem,
measured_nodes = unique(c(names(toy_metabolic_input),
                          names(toy_signaling_input))),
omnipath_ptm = omnipath_ptm)
```

`gmt_to_dataframe` *Convert gmt file to data frame*

Description

This function is designed to convert a gmt file (gene set file from MSigDB) into a two column data frame where the first column corresponds to omic features (genes) and the second column to associated terms (pathway the gene belongs to). One gene can belong to several pathways.

Usage

```
gmt_to_dataframe(gmtfile)
```

Arguments

`gmtfile`	a full path name of the gmt file to be converted

Value

a two column data frame where the first column corresponds to omic features and the second column to associated terms (pathways).

`load_tf_regulon_dorothea`
load transcription factor regulon

Description

load the transcription factors from `DOROTHEA` package and converts gene symbols to EntrezID using org.Hs.eg.db

Usage

```
load_tf_regulon_dorothea(toEntrez = TRUE, confidence = c("A", "B", "C"))
```

Arguments

toEntrez	if TRUE (default), converts gene symbols to EntrezID
confidence	strong vector (by default: c("A","B","C")). Subset of {A, B, C, D, E}. See the 'dorothea' for the meaning of confidence levels. package for further details.

Value

returns a PKN of a form of a data table. Each row is an interaction. Columns names are:

- 'tf' transcription factor - 'confidence' class of confidence - 'target' target gene - 'sign' indicates if interaction is up (1) or down-regulation (-1).

Examples

```
load_tf_regulon_dorothea()
```

---

load_tf_regulon_dorothea_omnipath

load_tf_regulon_dorothea_omnipath

Description

downloads the TF-regulons from Omnipaht. Different from DOROTHEA regulon because sign is handled differently: if both stimulation and inhibition was reported then it is removed.

Usage

```
load_tf_regulon_dorothea_omnipath()
```

Value

TF - TF-target interactions in tibble format.

Examples

```
load_tf_regulon_dorothea_omnipath()
```

metabolite_to_pubchem *Metabolite-PubChem CID Mapping*

Description

Mapping between metabolite names and PubChem CIDs obtained from the recon3D metabolic model. Combined table version from the recon3D matlab object.

Usage

```
data(metabolite_to_pubchem)
```

Format

An object of class "`data.frame`" with 1131 rows (metabolites) and two variables:

`name` Metabolite name synonym

`pubchem` Pubchem CID

Source

https://www.vmh.life/#downloadview, downloaded on Feb 19th, 2018.

References

Brunk, E. et al. (2018) *Nature Biotechnology*. **36**(3), 272–281.

Examples

```
data(metabolite_to_pubchem)
```

meta_network *Meta Prior Knowledge Network*

Description

Comprehensive Prior Knowledge Network (PKN), which combines signaling and metabolic interaction networks. The network was constructed using the Recon3D and STITCH metabolic networks as well as the signaling network from OmniPath.

Usage

```
data(meta_network)
```

Format

An object of class "tibble" with 117065 rows (interactions) and three variables:

`source` Source node, either metabolite or protein

`interaction` Type of interaction, 1 = Activation, -1 = Inhibition

`target` Target node, either metabolite or protein A detailed description of the identifier formatting can be found under https://metapkn.omnipathdb.org/00__README.txt.

Source

The network is available in Omnipath: https://metapkn.omnipathdb.org/metapkn__20200122.txt, the scripts used for the build of the network are available under https://github.com/saezlab/Meta_PKN.

References

Dugourd, A., Kuppe, C. and Sciacovelli, M. et. al. (2021) *Molecular Systems Biology*. **17**, e9730.

Examples

```
data(meta_network)
```

---

omnipath_ptm *OmniPath PTMs*

Description

Collection of annotated enzyme-substrate post translational modifications obtained from OmniPath.

Usage

```
data(omnipath_ptm)
```

Format

An object of class "data.frame" with 39201 rows (PTMs) and 12 variables:

`enzyme`

`substrate`

`enzyme_genesymbol`

`substrate_genesymbol`

`residue_type`

`residue_offset`

`modification`

sources

references

curation_effort

n_references

n_resources

Source

Default resource collection of OmniPath: http://omnipathdb.org/ptms?fields=sources,references&genesymbols=1, version of Feb 5th, 2020.

References

Turei, D., Korcsmaros, T. and Saez-Rodriguesz, J. (2016) *Nature Methods*. **13**(12), 966–967.

Examples

```
data(omnipath_ptm)
```

---

prepare_metabolomics_data

format COSMOS metabolic input

Description

This function prepares the metabolic data to be used in the COSMOS optimization steps. It takes as input a vector with the metabolic data (e.g, limma t values) named with PUBCHEM IDs and expand it to the multi-compartment COSMOS format. It also messages the number of final inputs in the meta network.

Usage

```
prepare_metabolomics_data(metabolic_data, meta_network)
```

Arguments

metabolic_data	A named numeric vector, containing the values to be used for the metabolic layer in COSMOS. The names of the vector should be PUBCHEM IDs.
meta_network	Prior knowledge network created with data(meta_network).

Value

A new vector ready to be used as COSMOS input.

Examples

```
# generate random t-values:
t_values <- rnorm(10)
# assign to metabolites with pubchem names
data(metabolite_to_pubchem)
names(t_values) <- names(metabolite_to_pubchem)[1:10]

data(meta_network)
prepare_metabolomics_data(t_values, meta_network)
```

`preprocess_COSMOS_metabolism_to_signaling` *Preprocess COSMOS Inputs For Metabolism to Signaling*

Description

Runs checks on the input data and simplifies the prior knowledge network. Simplification includes the removal of (1) nodes that are not reachable from signaling nodes and (2) interactions between transcription factors and target genes if the target gene does not respond or the response is contradictory with the change in the transcription factor activity. Optionally, further TF activities are estimated via network optimization via CARNIVAL and the interactions between TF and genes are filtered again.

Usage

```
preprocess_COSMOS_metabolism_to_signaling(
  meta_network = meta_network,
  tf_regulon = load_tf_regulon_dorothea(),
  signaling_data,
  metabolic_data,
  diff_expression_data,
  diff_exp_threshold = 1,
  maximum_network_depth = 8,
  expressed_genes = names(diff_expression_data)[!is.na(diff_expression_data)],
  remove_unexpressed_nodes = TRUE,
  filter_tf_gene_interaction_by_optimization = TRUE,
  CARNIVAL_options = default_CARNIVAL_options()
)
```

Arguments

`meta_network`	prior knowledge network (PKN). A PKN released with COSMOS and derived from Omnipath, STITCHdb and Recon3D can be used. See details on the data `meta_network`.
`tf_regulon`	collection of transcription factor - target interactions. A default collection from dorothea can be obtained by the `load_tf_regulon_dorothea` function.

signaling_data numerical vector, where names are signaling nodes in the PKN and values are from {1, 0, -1}. Continuous data will be discretized using the sign function.

metabolic_data numerical vector, where names are metabolic nodes in the PKN and values are continuous values that represents log2 fold change or t-values from a differential analysis. These values are compared to the simulation results (simulated nodes can take value -1, 0 or 1)

diff_expression_data
(optional) numerical vector that represents the results of a differential gene expression analysis. Names are gene names using EntrezID starting with an X and values are log fold change or t-values. convert_genesymbols_to_entrezid can be used for conversion. We use the "diff_exp_threshold" parameter to decide which genes changed significantly. Genes with NA values are considered none expressed and they will be removed from the TF-gene expression interactions.

diff_exp_threshold
threshold parameter (default 1) used to binarize the values of "diff_expression_data".

maximum_network_depth
integer > 0 (default: 8). Nodes that are further than "maximum_network_depth" steps from the signaling nodes on the directed graph of the PKN are considered non-reachable and are removed.

expressed_genes
character vector. Names of nodes that are expressed. By default we consider all the nodes that appear in diff_expression_data with a numeric value (i.e. nodes with NA are removed)

remove_unexpressed_nodes
if TRUE (default) removes nodes from the PKN that are not expressed, see input "expressed_genes".

filter_tf_gene_interaction_by_optimization
(default:TRUE), if TRUE then runs a network optimization that estimates TF activity not included in the inputs and checks the consistency between the estimated activity and change in gene expression. Removes interactions where TF and gene expression are inconsistent

CARNIVAL_options
list that controls the options of CARNIVAL. See details in default_CARNIVAL_options.

Value

cosmos_data object with the following fields:

meta_network Filtered PKN

tf_regulon TF - target regulatory network

signaling_data_bin Binarised signaling data

metabolic_data Metabolomics data

diff_expression_data_bin Binarized gene expression data

optimized_network Initial optimized network if filter_tf_gene_interaction_by_optimization is TRUE

See Also

meta_network for meta PKN, load_tf_regulon_dorothea for tf regulon, convert_genesymbols_to_entrezid for gene conversion, runCARNIVAL.

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_back <- preprocess_COSMOS_metabolism_to_signaling(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
```

---

preprocess_COSMOS_signaling_to_metabolism

Preprocess COSMOS Inputs For Signaling to Metabolism

Description

Runs checks on the input data and simplifies the prior knowledge network. Simplification includes the removal of (1) nodes that are not reachable from signaling nodes and (2) interactions between transcription factors and target genes if the target gene does not respond or the response is contradictory with the change in the transcription factor activity. Optionally, further TF activities are estimated via network optimization via CARNIVAL and the interactions between TF and genes are filtered again.

Usage

```
preprocess_COSMOS_signaling_to_metabolism(
  meta_network = meta_network,
  tf_regulon = load_tf_regulon_dorothea(),
  signaling_data,
  metabolic_data,
  diff_expression_data,
  diff_exp_threshold = 1,
  maximum_network_depth = 8,
  expressed_genes = names(diff_expression_data)[!is.na(diff_expression_data)],
  remove_unexpressed_nodes = TRUE,
  filter_tf_gene_interaction_by_optimization = TRUE,
  CARNIVAL_options = default_CARNIVAL_options()
)
```

Arguments

meta_network	prior knowledge network (PKN). A PKN released with COSMOS and derived from Omnipath, STITCHdb and Recon3D can be used. See details on the data meta_network.
tf_regulon	collection of transcription factor - target interactions. A default collection from dorothea can be obtained by the load_tf_regulon_dorothea function.
signaling_data	numerical vector, where names are signaling nodes in the PKN and values are from {1, 0, -1}. Continuous data will be discretized using the sign function.
metabolic_data	numerical vector, where names are metabolic nodes in the PKN and values are continuous values that represents log2 fold change or t-values from a differential analysis. These values are compared to the simulation results (simulated nodes can take value -1, 0 or 1)
diff_expression_data	(optional) numerical vector that represents the results of a differential gene expression analysis. Names are gene names using EntrezID starting with an X and values are log fold change or t-values. convert_genesymbols_to_entrezid can be used for conversion. We use the "diff_exp_threshold" parameter to decide which genes changed significantly. Genes with NA values are considered none expressed and they will be removed from the TF-gene expression interactions.
diff_exp_threshold	threshold parameter (default 1) used to binarize the values of "diff_expression_data".
maximum_network_depth	integer > 0 (default: 8). Nodes that are further than "maximum_network_depth" steps from the signaling nodes on the directed graph of the PKN are considered non-reachable and are removed.
expressed_genes	character vector. Names of nodes that are expressed. By default we consider all the nodes that appear in diff_expression_data with a numeric value (i.e. nodes with NA are removed)
remove_unexpressed_nodes	if TRUE (default) removes nodes from the PKN that are not expressed, see input "expressed_genes".
filter_tf_gene_interaction_by_optimization	(default:TRUE), if TRUE then runs a network optimization that estimates TF activity not included in the inputs and checks the consistency between the estimated activity and change in gene expression. Removes interactions where TF and gene expression are inconsistent
CARNIVAL_options	list that controls the options of CARNIVAL. See details in default_CARNIVAL_options.

Value

cosmos_data object with the following fields:

meta_network Filtered PKN

`tf_regulon` TF - target regulatory network

`signaling_data_bin` Binarised signaling data

`metabolic_data` Metabolomics data

`diff_expression_data_bin` Binarized gene expression data

`optimized_network` Initial optimized network if `filter_tf_gene_interaction_by_optimization` is `TRUE`

See Also

`meta_network` for meta PKN, `load_tf_regulon_dorothea` for tf regulon, `convert_genesymbols_to_entrezid` for gene conversion, `runCARNIVAL`.

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_for <- preprocess_COSMOS_signaling_to_metabolism(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
```

---

print.cosmos_data *Print Cosmos Data Summary Print a summary of cosmos data.*

Description

Print Cosmos Data Summary Print a summary of cosmos data.

Usage

```
## S3 method for class 'cosmos_data'
print(x, ...)
```

Arguments

`x`	`cosmos_data` object. Use the `preprocess_COSMOS_signaling_to_metabolism` or `preprocess_COSMOS_metabolism_to_signaling` functions to create one.
`...`	Further print arguments passed to or from other methods.

Value

input (invisible)

See Also

print, cosmos_data

`run_COSMOS_metabolism_to_signaling`
run COSMOS metabolism to signaling

Description

Runs COSMOS from metabolism to signaling. This function uses CARNIVAL to find a subset of the prior knowledge network based on optimization that (1) includes the most measured and input nodes and (2) which is in agreement with the data. Use `preprocess_COSMOS_metabolism_to_signaling` to prepare the the inputs, measurements and the prior knowledge network.

Usage

```
run_COSMOS_metabolism_to_signaling(
  data,
  CARNIVAL_options = default_CARNIVAL_options()
)
```

Arguments

`data`	`cosmos_data` object. Use the `preprocess_COSMOS_metabolism_to_signaling` function to create an instance.
`CARNIVAL_options`	List that controls the options of CARNIVAL. See details in `default_CARNIVAL_options`.

Value

List with the following elements:

`weightedSIF` The averaged networks found by optimization in a format of a Simple Interaction network, i.e. each row codes an edge

`N_networks` Number of solutions found by the optimization

`nodesAttributes` Estimated node properties

`individual_networks` List of optimial networks found

`individual_networks_node_attributes` Node activity in each network

See Also

`preprocess_COSMOS_metabolism_to_signaling`, `runCARNIVAL`, `cosmos_data`

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_back <- preprocess_COSMOS_metabolism_to_signaling(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
test_result_back <- run_COSMOS_metabolism_to_signaling(data = test_back,
CARNIVAL_options = CARNIVAL_options)
```

---

run_COSMOS_signaling_to_metabolism

run COSMOS signaling to metabolism

Description

Runs COSMOS from signaling to metabolism. This function uses CARNIVAL to find a subset of the prior knowledge network based on optimisation that (1) includes the most measured and input nodes and (2) which is in agreement with the data. Use `preprocess_COSMOS_signaling_to_metabolism` to prepare inputs, measurements and prior knowledge network.

Usage

```
run_COSMOS_signaling_to_metabolism(
  data,
  CARNIVAL_options = default_CARNIVAL_options()
)
```

Arguments

`data`	`cosmos_data` object. Use the `preprocess_COSMOS_signaling_to_metabolism` function to create an instance.
`CARNIVAL_options`	List that controls the options of CARNIVAL. See details in `default_CARNIVAL_options`.

Value

List with the following elements:

`weightedSIF` The averaged networks found by optimization in a format of a Simple Interaction network, i.e. each row codes an edge

`N_networks` Number of solutions found by the optimization

`nodesAttributes` Estimated node properties

`individual_networks` List of optimial networks found

`individual_networks_node_attributes` Node activity in each network

See Also

`preprocess_COSMOS_metabolism_to_signaling`, `runCARNIVAL`, `cosmos_data`

Examples

```
CARNIVAL_options <- cosmosR::default_CARNIVAL_options()
CARNIVAL_options$solver <- "lpSolve"
data(toy_network)
data(toy_signaling_input)
data(toy_metabolic_input)
data(toy_RNA)
test_for <- preprocess_COSMOS_signaling_to_metabolism(meta_network = toy_network,
signaling_data = toy_signaling_input,
metabolic_data = toy_metabolic_input,
diff_expression_data = toy_RNA,
maximum_network_depth = 15,
remove_unexpressed_nodes = TRUE,
CARNIVAL_options = CARNIVAL_options
)
test_result_for <- run_COSMOS_signaling_to_metabolism(data = test_for,
CARNIVAL_options = CARNIVAL_options)
```

---

toy_metabolic_input *Toy Metabolic Input Data*

Description

This metabolic data are a subset from the metabolic measurements used as an input in the case study of the COSMOS paper. The subset contains a random selection of metabolites present in the toy network.

Usage

```
data(toy_metabolic_input)
```

Format

An object of class "`numeric`" containing the t-values of 3 metabolites, which are named with metabolite PubChem CIDs matching the toy network.

Source

Subset of: https://github.com/saezlab/COSMOS_MSB/blob/main/data/metab_input_COSMOS.csv

References

Dugourd, A., Kuppe, C. and Sciacovelli, M. et. al. (2021) *Molecular Systems Biology*. **17**, e9730.

Examples

```
data(toy_metabolic_input)
```

---

toy_network *Toy Input Network*

Description

This signaling network is the reduced COSMOS network solution obtained in the case study of the COSMOS paper. Here, this network solution is reused as an exemplary input prior knowledge network (PKN).

Usage

```
data(toy_network)
```

Format

An object of class "`data.frame`" with 19 rows (interactions) and three variables:

`source` Source node, either metabolite or protein

`interaction` Type of interaction, 1 = Activation, -1 = Inhibition

`target` Target node, either metabolite or protein A detailed description of the identifier formatting can be found under https://metapkn.omnipathdb.org/00__README.txt.

Source

The network data are available on github: https://github.com/saezlab/COSMOS_MSB/tree/main/results/COSMOS_result/COSMOS_res_session.RData. The toy_network is the combined network of the COSMOS network solutions CARNIVAL_Result2 and CARNIVAL_Result_rerun subsequently reduced to 19 exemplary nodes.

References

Dugourd, A., Kuppe, C. and Sciacovelli, M. et. al. (2021) *Molecular Systems Biology*. **17**, e9730.

Examples

```
data(toy_network)
```

`toy_RNA` *Toy Input Transcription Data Set*

Description

This exemplary transcription data are the differential expression results analysed in the case study of the COSMOS paper.

Usage

```
data(toy_RNA)
```

Format

An object of class "`numeric`" containing the t-values of 15919 genes, which are named with gene Entrez IDs matching the toy network.

Source

https://github.com/saezlab/COSMOS_MSB/blob/main/data/RNA_ttop_tumorvshealthy.csv

References

Dugourd, A., Kuppe, C. and Sciacovelli, M. et. al. (2021) *Molecular Systems Biology*. **17**, e9730.

Examples

```
data(toy_RNA)
```

`toy_signaling_input` *Toy Signaling Input*

Description

This signaling data are a subset of the footprint-based signaling activity estimates of transcription factors, kinases and phophatases used as an input in the case study of the COSMOS paper. The subset contains a random selection of signaling proteins present in the toy network.

Usage

```
data(toy_signaling_input)
```

Format

An object of class "`data.frame`" containing the normalised enrichment scores (NES) of 2 signaling proteins, which are named with their respective gene Entrez ID matching the toy network.

Source

Subset of: https://github.com/saezlab/COSMOS_MSB/blob/main/data/signaling_input_COSMOS.csv

References

Dugourd, A., Kuppe, C. and Sciacovelli, M. et. al. (2021) *Molecular Systems Biology*. **17**, e9730.

Examples

```
data(toy_signaling_input)
```

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