

Package ‘cosmosR’

October 10, 2021

Type Package

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

Version 1.0.1

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 transcription factors and kinases and finds a network-level causal reasoning. Thereby, COSMOS provides mechanistic hypotheses for experimental observations across multi-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

RoxygenNote 7.1.1

VignetteBuilder knitr

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

Suggests testthat, knitr, rmarkdown

biocViews CellBiology, Pathways, Network, Proteomics, Metabolomics, Transcriptomics, GeneSignaling

git_url <https://git.bioconductor.org/packages/cosmosR>

git_branch RELEASE_3_13

git_last_commit 6d16ee7

git_last_commit_date 2021-06-22

Date/Publication 2021-10-10

Author Aurélien Dugourd [aut] (<<https://orcid.org/0000-0002-0714-028X>>),
Attila Gabor [aut] (<<https://orcid.org/0000-0002-0776-1182>>),
Katharina Zirngibl [cre, aut] (<<https://orcid.org/0000-0002-7518-0339>>)
Maintainer Katharina Zirngibl <katharina.zirngibl@uni-heidelberg.de>

R topics documented:

convert_ensembl_to_entrezid	2
convert_genesymbols_to_entrezid	3
cosmos_data	4
default_CARNIVAL_options	5
display_node_neighborhood	5
format_COSMOS_res	7
load_tf_regulon_dorothea	8
load_tf_regulon_dorothea_omnipath	9
metabolite_to_pubchem	9
meta_network	10
omnipath_ptm	11
prepare_metabolomics_data	12
preprocess_COSMOS_metabolism_to_signaling	12
preprocess_COSMOS_signaling_to_metabolism	15
print.cosmos_data	17
run_COSMOS_metabolism_to_signaling	18
run_COSMOS_signaling_to_metabolism	19
toy_metabolic_input	20
toy_network	21
toy_RNA	22
toy_signaling_input	22
Index	24

convert_ensembl_to_entrezid
<i>convert gene ensembl to entrez id</i>

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_neighborhood

display_node_neighborhood

Description

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

Usage

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

Arguments

<code>central_node</code>	character or character vector; node ID(s) around which a network will be branched out until measurements and input are reached
<code>sif</code>	df; COSMOS network solution in sif format, as returned by the <code>format_cosmos_res</code> function
<code>att</code>	df; attributes of the nodes of the COSMOS network solution, as returned by the <code>format_cosmos_res</code> function
<code>n</code>	numeric; maximum number of steps in the network to look for inputs and measurements

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_neighborhood(central_node = 'BCAT1',
sif = test_result_for[[1]],
att = test_result_for[[2]],
n = 5)
network_plot

```

format_COSMOS_res	<i>format_COSMOS_res</i>
-------------------	--------------------------

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)

```

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	<i>Meta Prior Knowledge Network</i>
--------------	-------------------------------------

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-Rodriguez, 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)
metabolite_to_pubchem <- metabolite_to_pubchem
names(t_values) <- metabolite_to_pubchem$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	<i>Print Cosmos Data Summary Print a summary of cosmos data.</i>
-------------------	--

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_metabolism_to_signaling function 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 optimal 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 optimal 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	<i>Toy Metabolic Input Data</i>
---------------------	---------------------------------

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	<i>Toy Input Network</i>
-------------	--------------------------

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	<i>Toy Input Transcription Data Set</i>
---------	---

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	<i>Toy Signaling Input</i>
---------------------	----------------------------

Description

This signaling data are a subset of the footprint-based signaling activity estimates of transcription factors, kinases and phosphatases 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)
```

Index

* datasets

- meta_network, [10](#)
- metabolite_to_pubchem, [9](#)
- omnipath_ptm, [11](#)
- toy_metabolic_input, [20](#)
- toy_network, [21](#)
- toy_RNA, [22](#)
- toy_signaling_input, [22](#)

convert_ensembl_to_entrezid, [2](#), [3](#)

convert_genesymbols_to_entrezid, [3](#), [3](#),
[13](#), [14](#), [16](#)

cosmos_data, [4](#), [4](#), [17–20](#)

default_CARNIVAL_options, [5](#), [14](#), [16](#), [18](#),
[19](#)

display_node_neighborhood, [5](#)

format_COSMOS_res, [7](#)

load_tf_regulon_dorothea, [4](#), [8](#), [13–16](#)

load_tf_regulon_dorothea_omnipath, [9](#)

meta_network, [4](#), [10](#), [13–16](#)

metabolite_to_pubchem, [9](#)

omnipath_ptm, [11](#)

prepare_metabolomics_data, [12](#)

preprocess_COSMOS_metabolism_to_signaling,
[4](#), [12](#), [17](#), [18](#), [20](#)

preprocess_COSMOS_signaling_to_metabolism,
[4](#), [15](#), [19](#)

print, [17](#)

print.cosmos_data, [17](#)

run_COSMOS_metabolism_to_signaling, [18](#)

run_COSMOS_signaling_to_metabolism, [19](#)

runCARNIVAL, [5](#), [14](#), [16](#), [18](#), [20](#)

sign, [4](#), [13](#), [15](#)

toy_metabolic_input, [20](#)

toy_network, [21](#)

toy_RNA, [22](#)

toy_signaling_input, [22](#)