

Package ‘pwOmics’

October 9, 2015

Type Package

Title Pathway-based data integration of omics data

Version 1.0.2

Date 2014-12-29

Author Astrid Wachter <Astrid.Wachter@med.uni-goettingen.de>

Maintainer Astrid Wachter <Astrid.Wachter@med.uni-goettingen.de>

Description pwOmics performs pathway-based level-specific data comparison of matching omics data sets based on pre-analysed user-specified lists of differential genes/transcripts and proteins. A separate downstream analysis of proteomic data including pathway identification and enrichment analysis, transcription factor identification and target gene identification is opposed to the upstream analysis starting with gene or transcript information as basis for identification of upstream transcription factors and regulators. The cross-platform comparative analysis allows for comprehensive analysis of single time point experiments and time-series experiments by providing static and dynamic analysis tools for data integration.

License GPL (>= 2)

Depends R (>= 3.2)

Imports data.table, rBiopaxParser, igraph, STRINGdb, graphics, gplots, Biobase, BiocGenerics, AnnotationDbi, biomaRt, AnnotationHub, GenomicRanges

Suggests ebdbNet, longitudinal, Mfuzz

biocViews SystemsBiology, Transcription, GeneTarget

NeedsCompilation no

R topics documented:

pwIntOmics-package	3
addFeedbackLoops	4

clusterTimeProfiles	4
createBiopaxnew	5
createIntIDs	6
dynamicConsensusNet	6
enrichPWs	8
enrichTFs	9
findxneighboroverlap	10
findxnextneighbors	10
genfullConsensusGraph	11
genGenelists	12
genGenelistssub	12
genIntIDs	13
getAliasfromSTRINGIDs	13
getAlias_Ensemble	14
getBiopaxModel	15
getbipartitegraphInfo	15
getConsensusSTRINGIDs	16
getDS_PWs	16
getDS_TFs	17
getDS_TGs	18
getFCsplines	19
getGenesIntersection	19
getOmicsallGeneIDs	20
getOmicsallProteinIDs	21
getOmicsDataset	22
getOmicsTimepoints	22
getProteinIntersection	23
getSTRING_graph	24
getTFIntersection	24
gettpIntersection	25
getUS_PWs	26
getUS_regulators	27
getUS_TFs	28
identifyPWs	29
identifyPWTFTGs	30
identifyRsofTFs	31
identifyTFs	32
identPWsofTFs	33
identRegulators	34
identTFs	34
identTFTGsInPWs	35
loadGenelists	35
loadPWs	36
OmicsExampleData	36
plotConsensusGraph	37
plodynConsensusNet	38
plotTimeProfileClusters	39
predictFCvals	40

preparePWinfo	40
print.OmicsData	41
PWidentallprots	41
PWidentallprotsub	42
PWidenttps	42
readOmics	43
readPWdata	44
readTFdata	45
readTFtargets	46
selectPWsofTFs	46
staticConsensusNet	47
SteinerTree_cons	48
TFidentallgenes	48
TFidenttps	49

Index	50
--------------	-----------

pwIntOmics-package	<i>Pathway-based data integration of omics data</i>
--------------------	---

Description

pwIntOmics performs pathway-based level-specific data comparison of matching omics data sets based on pre-analysed user-specified lists of differential genes/transcripts and proteins. A separate downstream analysis of proteomic data including pathway identification and enrichment analysis, transcription factor identification and target gene identification is opposed to the upstream analysis starting with gene or transcript information as basis for identification of upstream transcription factors and regulators. The cross-platform comparative analysis allows for comprehensive analysis of single time point experiments and time-series experiments by providing static and dynamic analysis tools for data integration.

Details

Package: pwIntOmics
 Type: Package
 Version: 1.0
 Date: 2014-12-29
 License: GLP-3

Author(s)

Astrid Wachter Maintainer: Astrid Wachter <Astrid.Wachter@med.uni-goettingen.de>

addFeedbackLoops *Add feedback loops from target genes to proteins/TFs if present.*

Description

Add feedback loops from target genes to proteins/TFs if present.

Usage

```
addFeedbackLoops(ST_net_targets)
```

Arguments

ST_net_targets full consensus graph.

Value

igraph object with feedback loops added.

clusterTimeProfiles *Clustering of time profiles.*

Description

Soft clustering of time series data with Mfuzz R package [1]. Filtering of genes with low expression changes possible via min.std parameter. Expression values are standardized and undergo fuzzy c-means clustering based on minimization of weighted square error function (see [2]). Fuzzifier parameter m is estimated via mestimate function of [1] based on a relation proposed by Schwaemmle and Jansen [3]. The optimal number of clusters is determined via the minimum distance between cluster centroid using Dmin function of [3]. Be aware that the cluster number determination might be difficult especially for short time series measurements.

Usage

```
clusterTimeProfiles(dynConsensusNet, min.std = 0, ncenters = 12)
```

Arguments

dynConsensusNet	result of dynamic analysis: inferred net generated by dynamicConsensusNet function.
min.std	threshold parameter to exclude genes with a low standard deviation. All genes with an expression smaller than min.std will be excluded from clustering. Default value is 0.
ncenters	integer specifying the maximum number of centers which should be tested in minimum distance between cluster centroid test; this number is used as initial number to determine the data-specific maximal cluster number based on number of distinct data points.

Value

output dataframe of mfuzz function.

References

1. L. Kumar and M. Futschik, Mfuzz: a software package for soft clustering of microarray data, *Bioinformatics*, 2(1) 5-7, 2007.
2. Bezdek JC, *Pattern Recognition with Fuzzy Objective Function Algorithms*, Plenum Press, New York, 1981.
3. Schwaemmle and Jensen, *Bioinformatics*, Vol. 26 (22), 2841-2848, 2010.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWFTGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)
dynConsNet = dynamicConsensusNet(data_omics, statConsNet)
clusterTimeProfiles(dynConsNet)

## End(Not run)
```

```
createBiopaxnew
```

Create a new Biopax model containing all database information.

Description

This function creates a new biopax model depending on which pathway databases are chosen for analysis.

Usage

```
createBiopaxnew(intIDs, pwdatabases)
```

Arguments

intIDs output list of genintIDs function.
 pwdatabases vector indicating with which pathway database the pathways should be determined; possible choices are "biocarta", "kegg", "nci", "reactome".

Value

biopax object generated from the specified pathway databases.

createIntIDs *Create internal IDs.*

Description

Create new internal ids in biopax\$df:

Usage

```
createIntIDs(data_omics, PWinfo)
```

Arguments

data_omics OmicsData object.
 PWinfo pathway database information from chosen pathway databases as from load-PWs.

Value

list of internal IDs from specified pathway databases.

dynamicConsensusNet *Dynamic analysis.*

Description

Generates continuous data for dynamic analysis of protein, TF and gene data via smoothing splines. 50 time points are generated this way. The following nodes are considered: Nodes which are part of the static consensus graphs from corresponding time points of the two different measurement types. In case a node is not significantly changed at a certain point in time its FC is assumed to remain constant at this time point. Calculation of the dynamic consensus net parameters are based on the ebdbNet R package [1]. The number of time points generated via smoothing splines (50) is based on their results for median AUCs of ROC curves. The number of forward time units a node is assumed to influence other nodes can be specified via the laghankel parameter. The cutoff determining the percent of total variance explained by the singular values generated by singular value decomposition (SVD) of the block-Hankel matrix H in order to specify the hidden state dimension K (for further details see [1]).

Usage

```
dynamicConsensusNet(data_omics, consensusGraphs, laghankel = 3,
  cutoffhankel = 0.9, conv.1 = 0.15, conv.2 = 0.05, conv.3 = 0.05,
  verbose = TRUE, max.iter = 100, max.subiter = 200)
```

Arguments

data_omics	OmicsData object.
consensusGraphs	result from static analysis: consensus graph generated by staticConsensusNet function.
laghankel	integer specifying the maximum relevant time lag to be used in constructing the block-Hankel matrix.
cutoffhankel	cutoff to determine desired percent of total variance explained; default = 0.9 as in [1].
conv.1	value of convergence criterion 1; default value is 0.15 (for further details see [1]).
conv.2	value of convergence criterion 2; default value is 0.05 (for further details see [1]).
conv.3	value of convergence criterion 3; default value is 0.05 (for further details see [1]).
verbose	boolean value, verbose output TRUE or FALSE
max.iter	maximum overall iterations; default value is 100 (for further details see [1]).
max.subiter	maximum iterations for hyperparameter updates; default value is 200 (for further details see [1]).

Value

list of 2 elements: 1) output parameters of dynamic network inference with ebdbNet package 2) splines data generated.

References

1. A. Rau, F. Jaffrezic, J.-L. Foulley, R. W. Doerge (2010). An empirical Bayesian method for estimating biological networks from temporal microarray data. *Statistical Applications in Genetics and Molecular Biology*, vol. 9, iss. 1, article 9.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
  TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
```

```

data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)
dynamicConsensusNet(data_omics, statConsNet)

## End(Not run)

```

enrichPWs

Pathway enrichment - downstream analysis.

Description

This function does pathway enrichment for pathways determined via identifyPWs function.

Usage

```
enrichPWs(data_omics, method = "BH", alpha = 0.05, ...)
```

Arguments

data_omics	OmicsData object.
method	correction method for multiple testing correction as specified in p.adjust documentation; default is Benjamini & Hochberg correction.
alpha	significance level for pathway enrichment; default is alpha = 0.05.
...	further input parameters for multiple comparison adjustment.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,

```



```

loadgenelists = "Genelists")

## Not run:
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)

## End(Not run)

```

enrichTFs

Transcription factor enrichment - upstream analysis.

Description

This function does transcription factor enrichment for transcription factor identified to be upstream of the diff. expressed genes/transcripts in the omics data set imported with readOmics function. In order to use this function first read in the transcription factor target gene information via readTFdata and identify the upstream TFs of the differentially expressed genes/transcripts with the identifyTFs function.

Usage

```
enrichTFs(data_omics, method = "BH", alpha = 0.05, ...)
```

Arguments

data_omics	OmicsData object.
method	correction method for multiple testing correction as specified in p.adjust documentation; default is Benjamini & Hochberg correction.
alpha	significance level for transcription factor enrichment; default is alpha = 0.05.
...	further input parameters for multiple comparison adjustment.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

setwd(system.file("extdata", package = "pwOmics"))
data_omics = readTFdata(data_omics)

```

```

data_omics_plus = readPWdata(data_omics,
loadgenelists = "Genelists")

## Not run:
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichTFs(data_omics)

## End(Not run)

```

`findxneighborsoverlap` *Find overlap of next neighbors of transcription factors in identified pathways.*

Description

Find the overlap of x next neighbors of transcription factors in identified pathways. Writes the overlap into a given list called 'regulators'.

Usage

```
findxneighborsoverlap(neighbors, noTFs_inPW, regul)
```

Arguments

<code>neighbors</code>	list of x next neighbors for each transcription factor in the pathway as provided by <code>findxnextneighbors</code> function.
<code>noTFs_inPW</code>	numeric value specifying number of TFs being at least part of the pathway.
<code>regul</code>	list element of regulators list for current pathway.

Value

list of regulators identified in x next neighbors of TFs.

`findxnextneighbors` *Find next neighbors of transcription factors in identified pathways.*

Description

Produces a list of x next neighbors for each transcription factor in the pathway.

Usage

```
findxnextneighbors(data_omics, pws_morex_TFs, pwxTFs, order_neighbors)
```

Arguments

<code>data_omics</code>	OmicsData object.
<code>pws_morex_TFs</code>	list of transcription factors in identified pathways.
<code>pwxTFs</code>	numeric variable of pathway currently investigated (from <code>pws_morexTFs</code>).
<code>order_neighbors</code>	integer specifying the order of the neighborhood: order 1 is TF plus its immediate neighbors.

Value

list of x next neighbors for each TF in the pathway.

`genfullConsensusGraph` *Combine SteinerNet with bipartite graph to get full consensus network.*

Description

Combine SteinerNet with bipartite graph to get full consensus network.

Usage

```
genfullConsensusGraph(ST_net, ST_TFTG)
```

Arguments

<code>ST_net</code>	steiner tree graph generated by <code>SteinerTree_cons</code> function.
<code>ST_TFTG</code>	steiner tree graph extended with consensus target genes and the edges between TFs and target genes.

Value

igraph object of network comprising steiner tree graph and TF - target gene interactions.

genGenelists *Generate genelists from pathway databases.*

Description

This function generates genelists from the chosen pathway databases for further processing in det-Pathways function.

Usage

```
genGenelists(intIDs, pwdatabases)
```

Arguments

intIDs	list containing Biopax model with newly generated internal IDs as processed with genintIDs function. The components of the list are biopax models for "biocarta", "kegg", "nci", "reactome". In case a database was not chosen the list entry contains a NA.
pwdatabases	vector indicating with which pathway database the pathways should be determined; possible choices are "biocarta", "kegg", "nci", "reactome".

Value

list of genelists of specified pathway databases.

genGenelistssub *Generate internally genelists from pathway databases.*

Description

This function generates genelists for a particular pathway database for further processing in det-Pathways function.

Usage

```
genGenelistssub(intIDs, database_int, PWDB_name)
```

Arguments

intIDs	list containing Biopax model with newly generated internal IDs as processed with genintIDs function. The components of the list are biopax models for "biocarta", "kegg", "nci", "reactome". In case a database was not chosen the list entry contains a NA.
database_int	integer indicating database entry in indIDs (output of genintIDs); biocarta = 1, kegg = 2, nci = 4, reactome = 4.
PWDB_name	character; pathway database name.

Value

data.table of genelist of particular pathway database.

genIntIDs	<i>Internal function for generation of pathway database specific internal IDs.</i>
-----------	--

Description

Generates new internal ids (database-specific) in biopax\$df.

Usage

```
genIntIDs(data_omics, PWinfo, PWinfo_ind, PWDBname)
```

Arguments

data_omics	OmicsData object.
PWinfo	pathway database information from chosen pathway databases as from load-PWs.
PWinfo_ind	integer specifying element of loadPWs output matching the chosen pathway database.
PWDBname	character; pathway database name.

Value

data.table with newly generated internal IDs of biopax model.

getAliasfromSTRINGIDs	<i>Map alias names to STRING IDs of consensus graph.</i>
-----------------------	--

Description

Map alias names to STRING IDs of consensus graph.

Usage

```
getAliasfromSTRINGIDs(data_omics, ST_net, consSTRINGIDs, tps, string_db)
```

Arguments

data_omics	OmicsData object.
ST_net	steiner tree graph generated by SteinerTree_cons function.
consSTRINGIDs	first element of list generated by getConsensusSTRINGIDs function; a data.frame including the proteins to be considered as terminal nodes in Steiner tree with col-names ST_proteins and the corresponding STRING IDs in column 'STRING_id'.
tps	integer specifying current timepoint under consideration.
string_db	second element of list generated by getConsensusSTRINGIDs function; species table (for human) of STRING database.

Value

igraph object with alias name annotation.

getAlias_Ensemble *Get Gene Symbols from Ensemble Gene Accession IDs.*

Description

Get Gene Symbols from Ensemble Gene Accession IDs.

Usage

```
getAlias_Ensemble(ids)
```

Arguments

ids	vector of Ensemble Gene Accession IDs.
-----	--

Value

ids character vector of gene symbols.

getBiopaxModel *Get upstream regulators of identified transcription factors.*

Description

Get upstream regulators of identified transcription factors.

Usage

```
getBiopaxModel(data_omics)
```

Arguments

data_omics OmicsData object.

Value

biopax model generated as consensus biopax models from all pathway databases selected for analysis.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta"),
  TFtargetdatabase = c("chea"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
  loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
getBiopaxModel(data_omics)

## End(Not run)
```

getbipartitegraphInfo *Get TF-target gene information for the consensus graph.*

Description

Get TF-target gene information for the consensus graph.

Usage

```
getbipartitegraphInfo(data_omics, tps)
```

Arguments

data_omics OmicsData object.
tps integer specifying current timepoint under consideration.

Value

list of transcription factor target gene interactions.

getConsensusSTRINGIDs *Get consensus graph in STRING IDs.*

Description

Get consensus graph in STRING IDs.

Usage

```
getConsensusSTRINGIDs(data_omics, tps, string_db)
```

Arguments

data_omics OmicsData object.
tps integer specifying current timepoint under consideration.
string_db STRING_db object.

Value

igraph object consensus graph with STRING IDs (only including proteins and transcription factors).

getDS_PWs *Get downstream analysis pathways.*

Description

This function returns pathways identified in the downstream analysis containing the significantly abundant proteins.

Usage

```
getDS_PWs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of protein time points, each element containing a data frame with the pathway IDs in the generated biopax model, corresponding pathway names and flags if those pathways are enriched (1 = enriched, NA = not enriched).

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
getDS_PWs(data_omics)

## End(Not run)
```

getDS_TFs

Get downstream analysis transcription factors in pathways.

Description

This function returns the genes identified in the downstream analysis and a column indicating if the genes are transcription factors.

Usage

```
getDS_TFs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of protein time points, each element containing a character vector with identified transcription factors.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyPWTFGs(data_omics, only_enriched = FALSE)
getDS_TFs(data_omics)

## End(Not run)
```

getDS_TGs

Get downstream analysis target genes of TFs found in pathways.

Description

Get downstream analysis target genes of TFs found in pathways.

Usage

```
getDS_TGs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of protein time points, each element containing a character vector with identified target genes.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
```

```

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
getDS_TGs(data_omics)

## End(Not run)

```

getFCsplines *Get fold change splines.*

Description

Calculate the splines used for the dynamic analysis.

Usage

```
getFCsplines(data_omics, nodes, nodetype)
```

Arguments

data_omics	OmicsData object.
nodes	character vector of nodes the fold change splines should be calculated for.
nodetype	character indicating to calculate splines for "proteins" or "genes".

Value

splines values used in dynamic analysis.

getGenesIntersection *Get genes intersection for the omics data on the different time points.*

Description

Get genes intersection for the omics data on the different time points.

Usage

```
getGenesIntersection(data_omics, tp_prot, tp_genes)
```

Arguments

data_omics	OmicsData object.
tp_prot	numeric integer defining protein timepoint measurement chosen for comparison.
tp_genes	numeric integer defining gene/transcript timepoint measurement chosen for comparison.

Value

list with three elements: 1) character vector of gene IDs identified in both upstream and downstream analysis 2) protein time point 3) gene/transcript time point.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWFTGs(data_omics, only_enriched = FALSE)
getGenesIntersection(data_omics, tp_prot = 4, tp_genes = 4)

## End(Not run)
```

```
getOmicsallGeneIDs      Get all gene IDs.
```

Description

This function returns the gene IDs of all genes (transcripts) measured.

Usage

```
getOmicsallGeneIDs(data_omics)
```

Arguments

data_omics	OmicsData object.
------------	-------------------

Value

all gene IDs.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))
getOmicsallGeneIDs(data_omics)
```

`getOmicsallProteinIDs` *Get all protein IDs.*

Description

This function returns the protein IDs of all proteins measured.

Usage

```
getOmicsallProteinIDs(data_omics)
```

Arguments

`data_omics` OmicsData object.

Value

all protein IDs.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))
getOmicsallProteinIDs(data_omics)
```

getOmicsDataset *Get Omics dataset.*

Description

This function returns the omics datasets of the experiment.

Usage

```
getOmicsDataset(data_omics, writeData = FALSE)
```

Arguments

data_omics OmicsData object.
writeData boolean value indicating if datasets should be written into csv file.

Value

list with protein data set as first element and gene data set as second element; both elements contain matrices with significant proteins/ genes/transcripts at the given time points.

Examples

```
data(OmicsExampleData)  
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),  
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,  
PWdatabase = c("biocarta"),  
TFtargetdatabase = c("chea"))  
getOmicsDataset(data_omics)
```

getOmicsTimepoints *Get Omics timepoints.*

Description

This function returns the timepoints of the OmicsData.

Usage

```
getOmicsTimepoints(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of protein time points and gene time points; in case of single time point measurement experiment number entered in OmicsData object.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta"),
  TFtargetdatabase = c("chea"))
getOmicsTimepoints(data_omics)
```

```
getProteinIntersection
```

Get protein intersection for the omics data on the different time points.

Description

The timepoints or measurement names for comparison have to be defined in `tp_prot` and `tp_genes` as given in the `readOmics` function.

Usage

```
getProteinIntersection(data_omics, tp_prot, tp_genes)
```

Arguments

<code>data_omics</code>	OmicsData object.
<code>tp_prot</code>	numeric integer defining protein timepoint measurement chosen for comparison.
<code>tp_genes</code>	numeric integer defining gene/transcript timepoint measurement chosen for comparison.

Value

list with three elements: 1) character vector of protein IDs identified in both upstream and downstream analysis 2) protein time point 3) gene/transcript time point.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
  TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
```

```

data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
getProteinIntersection(data_omics, tp_prot = 4, tp_genes = 4)

## End(Not run)

```

getSTRING_graph *Generate STRING PPI graph.*

Description

Generates connected graph with undirected edges from STRING PPI-database.

Usage

```
getSTRING_graph(string_db)
```

Arguments

string_db STRING_db object generated by getConsensusSTRINGIDs function.

Value

igraph object connected graph from STRING PPI database.

getTFIntersection *Get TF intersection for the omics data on the different time points.*

Description

Get TF intersection for the omics data on the different time points.

Usage

```
getTFIntersection(data_omics, tp_prot, tp_genes, only_enriched = TRUE)
```


Arguments

data_omics	OmicsData object.
tp_prot	numeric integer defining protein timepoint measurement chosen for comparison.
tp_genes	numeric integer defining gene/transcript timepoint measurement chosen for comparison.
only_enriched	Boolean value defining if transcription factors should be identified only for enriched pathways (TRUE); or for all identified pathways (FALSE); default is TRUE.

Value

list with three elements: 1) character vector of transcription factor IDs identified in both upstream and downstream analysis 2) protein time point 3) gene/transcript time point.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
getTFIntersection(data_omics, 4,4,only_enriched = TRUE)

## End(Not run)
```

gettpIntersection *Get omics data intersection on the three levels.*

Description

Get intersection for the omics data on all three levels (proteins, TFs, genes) on corresponding time points.

Usage

```
gettpIntersection(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list with three elements: 1) protein intersection 2) transcription factor intersection 3) gene intersection each element contains a list with overlapping time points of both upstream and downstream analyses.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFGs(data_omics, only_enriched = FALSE)
gettpIntersection(data_omics)

## End(Not run)
```

getUS_PWs

Get upstream pathways of identified transcription factors.

Description

Get upstream pathways of identified transcription factors.

Usage

```
getUS_PWs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of gene/transcript time points, each element containing a list of transcription factors; these transcription factor elements contain data frame with pathway IDs and pathway names.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
getUS_PWs(data_omics)

## End(Not run)
```

getUS_regulators

Get upstream regulators of identified transcription factors.

Description

Get upstream regulators of identified transcription factors.

Usage

```
getUS_regulators(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of gene/transcript time points, each element containing a vector of protein regulator IDs.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
getUS_regulators(data_omics)

## End(Not run)

```

getUS_TFs

Get upstream TFs.

Description

Get upstream TFs.

Usage

```
getUS_TFs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

list of length = number of gene/transcript time points, each element containing a data frame with upstream transcription factors and flag if these transcription factors are enriched (1 = enriched, NA = not enriched).

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))
## Not run:

```

```

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
getUS_TFs(data_omics)

## End(Not run)

```

identifyPWs	<i>Identify pathway IDs and pathway names of differentially abundant proteins</i>
-------------	---

Description

This function identifies the pathways of the differentially abundant proteins dependent on the chosen database. Requires rBiopaxParser package. Takes a lot of time for a high number of proteins and/or if all databases are chosen. First, chosen databases are loaded, then new internal pathway IDs are generated. Afterwards the genelists of the different databases are loaded or generated, depending on the loadgenelists option. After pathway identification for the reference time point, also pathway identification for different time points is performed. Pathway ID mapping takes some time, especially for such big databases as reactome, so use savegenelists and loadgenelists for easier and faster usage...

Usage

```
identifyPWs(data_omics_plus)
```

Arguments

`data_omics_plus`
output list of readPWdata function; first element contains an OmicsData object, seconds element the genelists data corresponding to the selected pathway database.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = "Genelists")

## Not run:
data_omics = identifyPWs(data_omics_plus)

## End(Not run)

```

identifyPWTFTGs	<i>Identify TFs in enriched pathways and their target genes - downstream analysis.</i>
-----------------	--

Description

This function identifies the transcription factors being part of the enriched pathways of downstream analysis. Subsequently it finds the target genes of these transcription factors from the selected TF-target gene database.

Usage

```
identifyPWTFTGs(data_omics, only_enriched = TRUE)
```

Arguments

data_omics	OmicsData object.
only_enriched	boolean value defining if transcription factors should be identified only for enriched pathways (TRUE); or for all identified pathways (FALSE); default is TRUE.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)

## Not run:
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
identifyPWTFTGs(data_omics, only_enriched = FALSE)

## End(Not run)

```

identifyRsofTFs	<i>Identify regulators of enriched transcription factors - upstream analysis.</i>
-----------------	---

Description

This function identifies the regulators upstream of the enriched/identified transcription factors in upstream analysis. Converting the pathway information to a regulatory graph needs some time... Warnings regarding the skipping of edges in building the regulatory graph can be ignored.

Usage

```

identifyRsofTFs(data_omics, only_enriched = TRUE, noTFs_inPW = 2,
order_neighbors = 6)

```

Arguments

data_omics	OmicsData object.
only_enriched	boolean value defining if transcription factors should be identified only for enriched pathways (TRUE); or for all identified pathways (FALSE); default is TRUE.
noTFs_inPW	integer; only regulators in upstream pathways with more than this number of TFs are identified.
order_neighbors	integer specifying the order of the neighborhood: order 1 is TF plus its immediate neighbors.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)

## Not run:
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
setwd(system.file("extdata/Genelists", package = "pwOmics"))
identifyRsofTFs(data_omics, only_enriched = FALSE, noTFs_inPW = 1,
order_neighbors = 10)

## End(Not run)
```

identifyTFs

Transcription factor identification.

Description

This function identifies the upstream transcription factors of the provided gene IDs.

Usage

```
identifyTFs(data_omics)
```

Arguments

data_omics OmicsData object.

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = "Genelists")

## Not run:
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)

## End(Not run)
```

identPWsofTFs	<i>Identification of pathways containing the transcription factors identified in upstream analysis</i>
---------------	--

Description

Identification of pathways containing the transcription factors identified in upstream analysis

Usage

```
identPWsofTFs(genelists, tps_TFs)
```

Arguments

genelists	data.table as read/loaded by loadGenelist function.
tps_TFs	data.table of upstream transcription factors and the flag for enrichment as returned from identTFs function.

Value

list with first element being a pathway list and second being a pathway dataframe of pathways including the TFs of the specified timepoint.

identRegulators	<i>Identify overlapping upstream regulators of x transcription factors</i>
-----------------	--

Description

Identify overlapping upstream regulators of x transcription factors

Usage

```
identRegulators(pws_morex_TFs, data_omics, order_neighbors, noTFs_inPW)
```

Arguments

pws_morex_TFs	list of transcription factors in identified pathways.
data_omics	OmicsData object.
order_neighbors	integer specifying the order of the neighborhood: order 1 is TF plus its immediate neighbors.
noTFs_inPW	integer; only regulators in upstream pathways with more than this number of TFs are identified.

Value

list of possible proteomic regulators.

identTFs	<i>This function provides a data.table of upstream transcription factors and the flag for enrichment.</i>
----------	---

Description

This function provides a data.table of upstream transcription factors and the flag for enrichment.

Usage

```
identTFs(data_omics, glen)
```

Arguments

data_omics	OmicsData object.
glen	numeric value; identifier for current timepoint.

Value

data.table of upstream TFs and an enrichment flag.

identTFTGsinPWs	<i>Prepare OmicsData object for pathway information.</i>
-----------------	--

Description

This function identifies the TFs in the pathway genes and determines their target genes on basis of the given (chosen) TF-target database(s).

Usage

```
identTFTGsinPWs(data_omics, temp_genelist)
```

Arguments

`data_omics` OmicsData object.
`temp_genelist` dataframe of unique gene IDs in enriched/not enriched PWs.

Value

list with first element being a genelist of the pathways and second being a target gene list of TFs.

loadGenelists	<i>Loading of genelists</i>
---------------	-----------------------------

Description

This function automatically loads the genelists corresponding to the selected pathway databases stored as RData file in the current working directory.

Usage

```
loadGenelists()
```

Value

genelist of specified pathway database.

loadPWs	<i>Load pathway database information.</i>
---------	---

Description

This function loads the pathway information from pathway databases. Needed in the identifyPWs function.

Usage

```
loadPWs(pwdatabases, biopax_level)
```

Arguments

pwdatabases	vector indicating with which pathway database the pathways should be determined; possible choices are "biocarta", "kegg", "nci", "reactome".
biopax_level	integer indicating biopax level of pathway database information to be retrieved.

Value

list of biopax model corresponding to specified pathway databases.

OmicsExampleData	<i>Omics example dataset.</i>
------------------	-------------------------------

Description

A dataset as input example for readOmics: A list containing two input lists, one for protein data, one for gene data, both including a vector of all measured IDs as first element and a list as second element including for each tp a dataframe with IDs and log foldchanges per timepoint.

Usage

```
data(OmicsExampleData)
```

Format

A list with a 'P' sublist containing protein data and a 'G' sublist containing gene/transcript data. Each of the sublists has a first element with all measured protein/gene IDs and a second element with a list of the length of the number of measured time points. Each of these lists contains a dataframe with a first column of significant protein/gene IDs at that time point and a second column with the corresponding logFCs.

Value

List with 2 sublists.

plotConsensusGraph *Plot consensus graph(s) from static analysis.*

Description

Consensus graph(s) plotted to pdf file stored in current working directory.

Usage

```
plotConsensusGraph(consensusGraphs, data_omics, ...)
```

Arguments

consensusGraphs	result from static analysis: consensus graph generated by staticConsensusNet function.
data_omics	OmicsData object.
...	further plotting/legend parameters.

Value

pdf file in current working directory.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWFTGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)
plot(statConsNet)

## End(Not run)
```

plotdynConsensusNet *Plot inferred net based on analysis analysis.*

Description

Dynamic analysis result is plotted to pdf file stored in current working directory.

Usage

```
plotdynConsensusNet(dynConsensusNet, sig.level, clarify = "TRUE",
  layout = layout.fruchterman.reingold, ...)
```

Arguments

dynConsensusNet	result of dynamic analysis: inferred net generated by dynamicConsensusNet function.
sig.level	significance level for plotting edges in network (between 0 and 1).
clarify	indicating if unconnected nodes should be removed; default = "TRUE".
layout	igraph layout parameter; default is layout.fruchterman.reingold.
...	further plotting/legend parameters.

Value

pdf file in current working directory.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
  TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
  loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
  noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)
dynConsNet = dynamicConsensusNet(data_omics, statConsNet)
plotdynConsensusNet(dynConsNet, sig.level = 0.8)

## End(Not run)
```

`plotTimeProfileClusters`*Plot time profile clusters of dynamic analysis result.*

Description

Plot time profile clusters of dynamic analysis result.

Usage

```
plotTimeProfileClusters(fuzzed_matsplines)
```

Arguments

```
fuzzed_matsplines      result of dynamic analysis: inferred net generated by dynamicConsensusNet
                        function.
...                    further plotting/legend parameters.
```

Value

pdf file in current working directory.

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = "Genelists")
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
data_omics = enrichPWs(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)
dynConsNet = dynamicConsensusNet(data_omics, statConsNet)
timeprof = clusterTimeProfiles(dynConsNet)
plotTimeProfileClusters(timeprof)

## End(Not run)
```

predictFCvals	<i>Prediction of continous data points via smoothing splines.</i>
---------------	---

Description

Prediction of continous data points via smoothing splines.

Usage

```
predictFCvals(data_omics, nopredpoints, splineslist, title)
```

Arguments

data_omics	OmicsData object.
nopredpoints	integer number; how many timpoints should be predicted?
splineslist	list of protein or gene nodes for which splines were generated: output of getFC-splines function.
title	character vector specifying name of title.

Value

list of splines matrix values and calculated times.

preparePWinfo	<i>Prepare OmicsData object for pathway information.</i>
---------------	--

Description

This function prepares the OmicsData object for the identified pathway information.

Usage

```
preparePWinfo(data_omics, plen)
```

Arguments

data_omics	OmicsData object.
plen	integer indicating the timepoint currently investigated.

Value

list of OmicsData object, current timepoint and pathways of interest.

print.OmicsData *Print an OmicsData object.*

Description

Print an OmicsData object.

Usage

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

Arguments

x an OmicsData object to print.
... further arguments to be passed to print.

Value

prints OmicsData object.

PWidentallprots *Identification of pathwayIDs and pathway names for all proteins.*

Description

Identification of pathwayIDs and pathway names for all proteins.

Usage

```
PWidentallprots(data_omics, genelists)
```

Arguments

data_omics OmicsData object.
genelists lists of genelists from chosen pathway databases.

Value

OmicsData object with identified pathway IDs for list of all proteins.

PWidentallprotssub *Internal subfunction for all protein pathway identification.*

Description

Internal subfunction for all protein pathway identification.

Usage

```
PWidentallprotssub(data_omics, genelists, genelist_ind, datab)
```

Arguments

data_omics	OmicsData object.
genelists	lists of genelists from chosen pathway databases
genelist_ind	integer specifying pathway database genelist matching; 1 = biocarta, 2 = kegg, 3 = nci, 4 = reactome.
datab	character vector indicating database name for message.

Value

OmicsData object with identified pathways for each protein.

PWidenttps *Identification of pathwayIDs and pathway names for proteins at individual timepoints.*

Description

Take the identified pathways from the list of all proteins and transfer this information for the individual timepoints.

Usage

```
PWidenttps(data_omics)
```

Arguments

data_omics	OmicsData object.
------------	-------------------

Value

data_omics OmicsData object with all pathways identified for the individual timepoints.

readOmics	<i>Read in omics data.</i>
-----------	----------------------------

Description

This function reads omics data: differentially expressed genes and relatively differentially abundant proteins with corresponding fold changes for each time point.

Usage

```
readOmics(tp_prots, tp_genes, omics, PWdatabase, TFtargetdatabase)
```

Arguments

tp_prots	numeric vector of protein timepoints used in experiment; in case of single time point experiments simply assign an experiment number (e.g. 1).
tp_genes	numeric vector of gene/transcript timepoints used in experiment; in case of single time point experiments simply assign an experiment number (e.g. 1).
omics	list containing protein and gene IDs and fold changes: Input are two lists, one for protein data, one for gene data, both including a vector of all measured IDs as first element and a list as second element including for each tp a dataframe with IDs and foldchanges per timepoint.
PWdatabase	character vector of pathway database names which should be used for pathway identification, possible choices are "biocarta", "kegg", "nci", "reactome".
TFtargetdatabase	character vector of TF target database names which should be used for transcription factor/target gene identification, possible choices are "chea", "pazar", "userspec". In case the user is able to provide an own list of transcription factor target gene matches, he can indicate this via "userspec".

Value

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
  PWdatabase = c("biocarta"),
  TFtargetdatabase = c("chea"))

## Not run:
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
  tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
```

```
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar", "userspec"))

## End(Not run)
```

readPWdata

Read in pathway database data needed for pathway identification.

Description

This function reads pathway data of the chosen database(s) via the AnnotationHub [1] package and rBiopaxParser [2] package. Takes a lot of time for a high number of proteins and/or if all databases are chosen. First, chosen databases are retrieved, then new internal pathway IDs are generated. Afterwards the genelists of the different databases are loaded or generated, depending on the loadgenelists option. Pathway ID mapping takes some time, especially for such big databases as reactome, so the genelists are automatically stored in the current working folder and can be used via loadgenelists in case you use this function again for easier and faster usage... Biopax level of retrieved databases is 2 by default.

Usage

```
readPWdata(data_omics, loadgenelists, biopax_level = 2)
```

Arguments

data_omics	OmicsData object.
loadgenelists	path of genelist RData files stored previously; all genelists stored in this path are read in and used automatically if path is given; if loadgenelists = FALSE, then genelists from pathway databases have to be generated first.
biopax_level	integer indicating biopax level of pathway database information. default level is 2.

Value

list of OmicsData object and genelists for selected pathway databases.

References

1. Morgan M, Carlson M, Tenenbaum D and Arora S. AnnotationHub: Client to access AnnotationHub resources. R package version 1.99.75.
2. Kramer F, Bayerlova M, Klemm F, Bleckmann A and Beissbarth T. rBiopaxParser - an R package to parse, modify and visualize BioPAX data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics, loadgenelists = "Genelists")
data_omics_plus[[2]][[1]]

```

readTFdata

Reads in chosen transcription factor target database information.

Description

This function reads in transcription factor information given the selected transcription factor target gene database. The database file(s) have to be stored in the current working directory. Usage of pazar database could take some time due to ID mapping. The individual pazar files have to be stored in a subfolder with name 'Pazar_tftargets'.

Usage

```
readTFdata(data_omics, TF_target_path)
```

Arguments

data_omics OmicsData object.

TF_target_path character vector indicating path of the txt file of matching transcription factors and target genes; the file should be a txt file with first column transcription factors and second column target gene symbols without a header.

Value

OmicsData object - a list containing information about the user data (timepoints, IDs, fold changes) and the selected databases chosen for the analysis.

OmicsData object: list of 4 elements (OmicsD, PathwayD, TFtargetsD, Status); OmicsD containing omics data set + results (after analysis); PathwayD containing selected pathway databases + biopax model; TFtargetsD containing selected TF target gene databases + TF target gene data.

Examples

```

data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta"),
TFtargetdatabase = c("chea"))

```

```
data_omics = readTFdata(data_omics)
data_omics[[3]]
```

readTFtargets *Read in matching transcription factor target gene pairs.*

Description

In case the user is able to provide a file with transcription factor - target gene matches (e.g. from TRANSFAC database) this function can read in the information. The file needs to be a txt file with first column transcription factors and second column target gene symbols without a header.

Usage

```
readTFtargets(data_omics, TF_target_path)
```

Arguments

data_omics OmicsData object.
TF_target_path path of txt file containing the transcription factor target gene information as specified above.

Value

data frame with user-specified TF target gene information.

selectPWsofTFs *Select pathways with more than x TFs*

Description

Select pathways with more than x TFs

Usage

```
selectPWsofTFs(pathway_list, pathway_frame, noTFs_inPW)
```

Arguments

pathway_list first element of list returned from identPWsofTFs function; contains a list of pathways.
pathway_frame second element of list returned from identPWsofTFs function; contains a data.frame of pathways.
noTFs_inPW numeric value specifying number of TFs being at least part of the pathway.

Value

list of pathways with more than x TFs.

staticConsensusNet *Static analysis.*

Description

Identify for each corresponding timepoint of the two datasets the consensus network. Protein intersection of the omics data and TF intersection are linked via SteinerTree algorithm applied on STRING protein-protein interaction database. The Steiner tree algorithm refers to the shortest path heuristic algorithm of [1,2]. Target genes of this consensus network are identified via the chosen TF-target gene database(s). Please note that the consensus graphs can be different as in the Steiner Tree algorithm the start terminal node is picked arbitrarily and there are always several shortest path distances.

Usage

```
staticConsensusNet(data_omics, run_times = 3)
```

Arguments

data_omics	OmicsData object.
run_times	integer specifying number of times to run SP Steiner tree algorithm to find minimal graph, default is 3.

Value

list of igraph objects; length corresponds to number of overlapping time points from upstream and downstream analysis.

References

1. Path heuristic and Original path heuristic, Section 4.1.3 of the book "The Steiner tree Problem", Peter L. Hammer
2. "An approximate solution for the Steiner problem in graphs", H Takahashi, A Matsuyama

Examples

```
#please run with whole database files (prepared according to vignette)
data(OmicsExampleData)
data_omics = readOmics(tp_prots = c(0.25, 1, 4, 8, 13, 18, 24),
tp_genes = c(1, 4, 8, 13, 18, 24), OmicsExampleData,
PWdatabase = c("biocarta", "kegg", "nci", "reactome"),
TFtargetdatabase = c("chea", "pazar"))
## Not run:
data_omics = readTFdata(data_omics)
data_omics_plus = readPWdata(data_omics,
loadgenelists = FALSE)
data_omics = identifyPWs(data_omics_plus)
data_omics = identifyTFs(data_omics)
```

```

data_omics = enrichPWS(data_omics)
data_omics = identifyRsofTFs(data_omics, only_enriched = FALSE,
noTFs_inPW = 1, order_neighbors = 10)
data_omics = identifyPWTFTGs(data_omics, only_enriched = FALSE)
statConsNet = staticConsensusNet(data_omics)

## End(Not run)

```

SteinerTree_cons *Steiner tree algorithm.*

Description

Use this function to get the Steiner tree based on the STRING protein-protein interaction database.

Usage

```
SteinerTree_cons(terminal_nodes, PPI_graph, run_times)
```

Arguments

`terminal_nodes` character vector of final nodes used for generation of Steiner tree.
`PPI_graph` igraph object; graph should be connected and have undirected edges.
`run_times` integer specifying number of times to run SP Steiner tree algorithm to find minimal graph.

Value

igraph object including Steiner tree.

TFidentallgenes *Identification of upstream transcription factors for all genes.*

Description

Identification of upstream transcription factors for all genes.

Usage

```
TFidentallgenes(data_omics)
```

Arguments

`data_omics` OmicsData object.

Value

`data_omics` OmicsData object with upstream TFs identified for all genes.

TFidenttps	<i>Identification of upstream transcription factors.</i>
------------	--

Description

Identification of upstream transcription factors for the differentially expressed genes of the different timepoints.

Usage

```
TFidenttps(data_omics)
```

Arguments

data_omics OmicsData object.

Value

data_omics OmicsData object with upstream TFs of differentially expressed genes for separate timepoints identified.

Index

*Topic **datasets**

OmicsExampleData, 36

*Topic **manip**

addFeedbackLoops, 4
clusterTimeProfiles, 4
createBiopaxnew, 5
createIntIDs, 6
dynamicConsensusNet, 6
enrichPWs, 8
enrichTFs, 9
findxneighboroverlap, 10
findxnextneighbors, 10
genfullConsensusGraph, 11
genGenelists, 12
genGenelistssub, 12
genIntIDs, 13
getAlias_Ensemble, 14
getAliasfromSTRINGIDs, 13
getBiopaxModel, 15
getbipartitegraphInfo, 15
getConsensusSTRINGIDs, 16
getDS_PWs, 16
getDS_TFs, 17
getDS_TGs, 18
getFCsplines, 19
getGenesIntersection, 19
getOmicsallGeneIDs, 20
getOmicsallProteinIDs, 21
getOmicsDataset, 22
getOmicsTimepoints, 22
getProteinIntersection, 23
getSTRING_graph, 24
getTFIntersection, 24
gettpIntersection, 25
getUS_PWs, 26
getUS_regulators, 27
getUS_TFs, 28
identifyPWs, 29
identifyPWTFs, 30

identifyRsofTFs, 31
identifyTFs, 32
identPWsofTFs, 33
identRegulators, 34
identTFs, 34
identTFTGsInPWs, 35
loadGenelists, 35
loadPWs, 36
plotConsensusGraph, 37
plotdynConsensusNet, 38
plotTimeProfileClusters, 39
predictFCvals, 40
preparePWinfo, 40
print.OmicsData, 41
PWidentallprots, 41
PWidentallprotssub, 42
PWidenttps, 42
readOmics, 43
readPWdata, 44
readTFdata, 45
readTFtargets, 46
selectPWsofTFs, 46
staticConsensusNet, 47
SteinerTree_cons, 48
TFidentallgenes, 48
TFidenttps, 49

*Topic **package**

pwIntOmics-package, 3

addFeedbackLoops, 4

clusterTimeProfiles, 4
createBiopaxnew, 5
createIntIDs, 6

dynamicConsensusNet, 6

enrichPWs, 8
enrichTFs, 9

findxneighboroverlap, 10

findnextneighbors, 10

genfullConsensusGraph, 11

genGenelists, 12

genGenelistssub, 12

genIntIDs, 13

getAlias_Ensemble, 14

getAliasfromSTRINGIDs, 13

getBiopaxModel, 15

getbipartitegraphInfo, 15

getConsensusSTRINGIDs, 16

getDS_PWs, 16

getDS_TFs, 17

getDS_TGs, 18

getFCsplines, 19

getGenesIntersection, 19

getOmicsallGeneIDs, 20

getOmicsallProteinIDs, 21

getOmicsDataset, 22

getOmicsTimepoints, 22

getProteinIntersection, 23

getSTRING_graph, 24

getTFIntersection, 24

gettpIntersection, 25

getUS_PWs, 26

getUS_regulators, 27

getUS_TFs, 28

identifyPWs, 29

identifyPWTFTGs, 30

identifyRsofTFs, 31

identifyTFs, 32

identPWsofTFs, 33

identRegulators, 34

identTFs, 34

identTFTGsinPWs, 35

loadGenelists, 35

loadPWs, 36

OmicsExampleData, 36

plotConsensusGraph, 37

plotdynConsensusNet, 38

plotTimeProfileClusters, 39

predictFCvals, 40

preparePWinfo, 40

print.OmicsData, 41

PWidentallprots, 41

PWidentallprotssub, 42

PWidenttps, 42

pwIntOmics (pwIntOmics-package), 3

pwIntOmics-package, 3

readOmics, 43

readPWdata, 44

readTFdata, 45

readTFtargets, 46

selectPWsofTFs, 46

staticConsensusNet, 47

SteinerTree_cons, 48

TFidentallgenes, 48

TFidenttps, 49