Package 'XINA'

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Type Package

Title Multiplexes Isobaric Mass Tagged-based Kinetics Data for Network Analysis

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Description The aim of XINA is to determine which proteins exhibit similar patterns within and across experimental conditions, since proteins with co-abundance patterns may have common molecular functions. XINA imports multiple datasets, tags dataset in silico, and combines the data for subsequent subgrouping into multiple clusters. The result is a single output depicting the variation across all conditions. XINA, not only extracts coabundance profiles within and across experiments, but also incorporates protein-protein interaction databases and integrative resources such as KEGG to infer interactors and molecular functions, respectively, and produces intuitive graphical outputs.

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Contents

`add_legend` *add_legend*

Description

Add plot legend and locate it outside of a network plot

Usage

```
add_legend(legend_location = "bottomright", ...)
```

Arguments

`legend_location`	Network centrality score matrix
`...`	Numeric, complex, or logical vectors.

Value

a legend to a plot

alluvial_enriched *alluvial_enriched*

Description

'alluvial_enriched' draws an alluvial plot and finds comigrated proteins. The comigration is a group of proteins that show the same expression pattern, classified and evaluated by XINA clustering, in at least two conditions. XINA can reduce the dataset complexity by filtering based on the number of comigrated proteins (size, 'comigration_size' parameter) and perform an enrichment test (P-value of Fisher's exact test, 'pval_threshold') to determine significance of enriched comigrations. The Fisher's exact test can only be done for two conditions at a time. The following 2x2 table was used to calculate the P-value from the Fisher's exact test. To evaluate significance of co-migrated proteins from cluster #1 in control to cluster #2 in test group,

-	cluster #1 in control	other clusters in control
cluster #2 in test	65 (TP)	175 (FP)
other clusters in test	35 (FN)	979 (TN)

Usage

```
alluvial_enriched(clustering_result, selected_conditions,
  comigration_size = 0, pval_threshold = 1, pval_method = "fdr",
  cex = 0.7, alpha = 0.3)
```

Arguments

clustering_result	A list containing XINA clustering results. See xina_clustering
selected_conditions	A vector of condition names used in XINA clustering results. The number of selected conditions should be at least two.
comigration_size	The number of proteins comigrated together in the selected conditions of XINA clustering results. Default is 0
pval_threshold	This option is avaiable only when you selected two conditions for comigration search.
pval_method	Method for p-value adjustment. See p.adjust
cex	Scaling of fonts of category labels. Default if 0.7. See alluvial
alpha	Transparency of the stripes. Default if 0.3. See alluvial

Value

A data frame containing comigrations and an alluvial plot showing comigrations

Examples

```
# load XINA example data
data(xina_example)

# Get the experimental conditions in the example data
classes <- as.vector(example_clusters$condition)

# Get comigrations without any thresholds
all_comigrations <- alluvial_enriched(example_clusters, classes)

# Get comigrations that have >= 5 size (the number of comigrated proteins)
all_cor_enriched <- alluvial_enriched(example_clusters, classes, comigration_size=5)

# Get all the comigrations between Control and Stimulus1
comigrations_Control_Stimulus1 <- alluvial_enriched(example_clusters,
c(classes[1],classes[2]))

# Get comigrations between Control and Stimulus1, that have >=5 size
comigrations_Control_Stimulus1_over5 <- alluvial_enriched(example_clusters,
c(classes[1],classes[2]), comigration_size=5)

# Get comigrations between Control and Stimulus1,
# that have >= 5 size and enrichment FDR <= 0.01
comigrations_Control_Stimulus1_pval0.01_size5 <- alluvial_enriched(example_clusters,
c(classes[1],classes[2]), comigration_size=5, pval_threshold=0.01)

# Get  comigrations between Control and Stimulus1,
# that have >= 5 size and enrichment Benjamini & Yekutieli <= 0.01
comigrations_Control_Stimulus1_BY0.01_size5 <- alluvial_enriched(example_clusters,
c(classes[1],classes[2]), comigration_size=5, pval_threshold=0.01, pval_method="BY")
```

`alluvial_enrichment_tests` *alluvial_enrichment_tests*

Description

Fisher's exact test to calculate the significance over all comigrations. The following 2x2 table was used to calculate p-value from Fisher's exact test. To evaluate significance of comigrated proteins from cluster #1 in control to cluster #2 in test condition,

	cluster #1 in control	**other clusters in control**
cluster #2 in test	65 (TP)	175 (FP)
other clusters in test	35 (FN)	979 (TN)

'alluvial_enrichment_tests' also provides another statistical methods including Hypergeometric test and Chi-square test.

Usage

```
alluvial_enrichment_tests(count_table, c1, c2, non_cluster = 0,
  test_type = "fisher")
```

Arguments

count_table	A data frame generated by using count.
c1	A selected cluster in the first condition.
c2	A selected cluster in the second condition.
non_cluster	The cluster number for proteins that were not detected in a specific sample. Default is 0.
test_type	Enrichment test type. 'fisher' = Fisher's exact test, 'hyper' = Hypergeometric test, 'chisq' = Chi-square test

Value

P-value of comigration enrichment test and 2x2 table information

---

calculate_centrality_scores *calculate_centrality_scores*

Description

'calculate_centrality_scores' computes network centrality scores

Usage

```
calculate_centrality_scores(net, centrality_type = "Degree")
```

Arguments

net	protein-protein interaction network of igraph
centrality_type	the maximum number of clusters

Value

A vector of network centrality scores

---

default_size *default_size*

Description

Calculate image size based on the number of clusters

Usage

```
default_size(max_cluster)
```

Arguments

max_cluster	the maximum number of clusters

Value

A vector of plot width and height

`draw_alluvial_plot` *draw_alluvial_plot*

Description

'draw_alluvial_plot' draw a alluvial plot

Usage

```
draw_alluvial_plot(clustering_result, selected_conditions, count_table,
  alluvia_colors = NULL, cex = 0.7, alpha = 0.3)
```

Arguments

`clustering_result`	A list containing XINA clustering results. See xina_clustering.
`selected_conditions`	A vector of condition names used in XINA clustering results. The number of selected conditions should be at least two.
`count_table`	A data frame generated by using count.
`alluvia_colors`	A vector containing the user-defined colors for each alluvium.
`cex`	Size of cluster number on block axis. Default if 0.7. See alluvial.
`alpha`	Transparency of alluvia colors. Default is 0.3. See alluvial.

Value

An alluvial plot displaying comigrations and the data frame containing the input count_table with colors.

Examples

```
# load XINA example data
data(xina_example)

# get a vector of experimental conditions analyzed in the clustering results
classes <- as.vector(example_clusters$condition)

comigrations_size_over5 <- alluvial_enriched(example_clusters, classes, comigration_size=5)
draw_alluvial_plot(example_clusters, classes, comigrations_size_over5)
```

`example_clusters` *Randomly generated example datasets for XINA users. A dataset containing the XINA clustering results.*

Description

- aligned. XINA clustering results aligned by conditions
- data_column. Column names for data matrix
- out_dir. Not available in this example dataset
- nClusters. The number of user-desired clusters. It's 30 in the example.
- max_cluster. The number of clusters found in the dataset. It's 21 in the example.
- chosen_model. The chosen covariance model for the example dataset. It's VEI in the example
- optimal_BIC. BIC at the optimized clustering. It's 29473.57 in the example
- condition. The experimental conditions in the dataset.
- color_for_condition. The default color for the conditions that will be used in XINA plot drawing.
- color_for_clusters. The default color for the clusters that will be used in XINA clustering plot.
- norm_method. The used normalization method to standardize the input data. It's "sum_normalization" in the example.

Format

A list with the example XINA clustering result

`extract_data_column` *extract_data_column*

Description

Extract data column names from XINA clustering result

Usage

```
extract_data_column(col_head_of_clustering)
```

Arguments

`col_head_of_clustering`
: Column names of XINA clustering result

Value

A vector containing column names of data matrix

find_similar_clusters *find_similar_clusters*

Description

Compare clusters and find similar ones

Usage

```
find_similar_clusters(clustering_result, threshold = 0.95)
```

Arguments

clustering_result	A list containing XINA clustering results. See xina_clustering
threshold	Pearson's r threshold to find similar ones

Value

Write a csv file containing similar clustering information based on the given Pearson's R threshold

generate_count_table *generate_count_table*

Description

Count the number of comigrated proteins using count

Usage

```
generate_count_table(clustering_result, selected_conditions,
  comigration_size)
```

Arguments

clustering_result	A list containing XINA clustering results. See xina_clustering
selected_conditions	A vector of condition names used in XINA clustering results.
comigration_size	The number of proteins comigrated together in the selected conditions of XINA clustering results. Default is 0.

Value

A data frame containing comigrations.

generate_superset *generate_superset*

Description

Merge input kinetics files

Usage

```
generate_superset(f_names, data_column, delim = ",",
  norm = "sum_normalization")
```

Arguments

f_names	A vector of .csv file paths containing kinetics data
data_column	A vector of column names containing data matrix
delim	The delimiter of input file (default is ',')
norm	The normalization method. It should be one of c('sum_normalization', 'zs-core'). Default is 'sum_normalization'.

Value

A data frame containing kinetics data obtained from files in the f_names vector

get_colors *get_colors*

Description

Generate color series for XINA graphics

Usage

```
get_colors(nClusters, set = "", colorset = NULL)
```

Arguments

nClusters	The number of clusters
set	Pre-defined color series set
colorset	manually defined color codes

Value

A vector for color code of XINA graphics

`get_color_for_nodes` *get_color_for_nodes*

Description

Pre-defined 30 colors

Usage

```
get_color_for_nodes()
```

Value

A vector for color code of XINA graphics

`get_comigrations_by_name` *get_comigrations_by_name*

Description

'get_comigrations_by_name' finds proteins comigrated with the given proteins

Usage

```
get_comigrations_by_name(clustering_result, selected_conditions,
  protein_list, cex = 0.7, alpha = 0.3)
```

Arguments

`clustering_result`	A list containing XINA clustering results. See xina_clustering
`selected_conditions`	A vector of condition names used in XINA clustering results. The number of selected conditions should be at least two.
`protein_list`	A vector containing gene names.
`cex`	Size of cluster number on block axis. Default if 0.7. See alluvial
`alpha`	Transparency of alluvia colors. Default is 0.3. See alluvial

Value

An alluvial plot displaying comigrations and the data frame containing comigrations of the input proteins

Examples

```
# load XINA example data
data(xina_example)

# the clustering result table
all_proteins  <- as.character(example_clusters$aligned$`Gene name`)
# get a vector of experimental conditions analyzed in the clustering results
classes <- as.vector(example_clusters$condition)

comigrated_prots_all <- get_comigrations_by_name(example_clusters, classes, all_proteins[1:3])
```

`get_condition_biased_comigrations` *get_condition_biased_comigrations*

Description

get comigrations that at least one biased cluster is involved in. Biased clusters are defined by

Usage

```
get_condition_biased_comigrations(clustering_result, count_table = NULL,
  selected_conditions, condition_composition, threshold_percent = 50,
  color_for_null = "gray", color_for_highly_matched = "red4",
  cex = 0.7, alpha = 0.3)
```

Arguments

`clustering_result`	A list containing XINA clustering results. See xina_clustering
`count_table`	A data frame generated by using count. If count_table is NULL (by default), XINA will consider all the comigrations.
`selected_conditions`	A vector of condition names used in XINA clustering results. The number of selected conditions should be at least two.
`condition_composition`	The resulting data frame of 'plot_condition_compositions'. See plot_condition_compositions.
`threshold_percent`	Default is 50. The percentage threshold for finding condition-biased clusters
`color_for_null`	A color for non-condition-biased comigrations. Default is 'gray'
`color_for_highly_matched`	A color for comigrations that are involved with more than two condition-biased clusters. Default is 'red4'
`cex`	Size of cluster number on block axis. Default if 0.7. See alluvial.
`alpha`	Transparency of alluvia colors. Default is 0.3. See alluvial.

Value

An alluvial plot displaying comigrations and the data frame containing condition-biased comigrations.

Examples

```
# load XINA example data
data(xina_example)

# get a vector of experimental conditions analyzed in the clustering results
conditions <- as.vector(example_clusters$condition)

# get condition composition information
condition_composition <- plot_condition_compositions(example_clusters)

comigrations_size10 <- alluvial_enriched(example_clusters, conditions, comigration_size=10)
# Finding condition-biased comigrations by 50% threshold
condition_biased_comigrations <-
get_condition_biased_comigrations(clustering_result=example_clusters,
count_table=comigrations_size10, selected_conditions=conditions,
condition_composition=condition_composition)

# Finding condition-biased comigrations by 70% threshold
condition_biased_comigrations <-
get_condition_biased_comigrations(clustering_result=example_clusters,
count_table=comigrations_size10, selected_conditions=conditions,
condition_composition=condition_composition,
threshold_percent=70)
```

`get_layout` *get_layout*

Description

Get igraph layout by the number of nodes

Usage

```
get_layout(subnet_condition)
```

Arguments

`subnet_condition`
: A igraph sub-network

Value

igraph network layout

get_mTOR_proteins *get_mTOR_proteins*

Description

Get mTOR pathway genes

Usage

```
get_mTOR_proteins(time_points, conditions)
```

Arguments

time_points	A vector containing time points of the data matrix
conditions	A vector containing condition information, for example normal, disease and drug treated disase.

Value

A vector containing mTOR pathway gene names

get_random_data *get_random_data*

Description

Get randomized time-series data

Usage

```
get_random_data(time_points, conditions, num_total, percent.sign = 0.1,
  equal = TRUE)
```

Arguments

time_points	A vector containing time points of the data matrix
conditions	A vector containing condition information, for example normal, disease and drug treated disase.
num_total	The number of total proteins to be generated
percent.sign	Percentage of differentially expressed proteins. Ignored when equal=FALSE.
equal	If equal is TRUE, all the conditions will have numbers between 0 and 1. If it is FALSE, the first three conditions will have different ranges. First condition will have numbers from 0.3 to 0.4. Second condition will have numbers from 0.6 to 0.8. Third condition will have numbers from 0.3 to 0.5. Other conditions will have numbers from 0 to 1.

Value

A list containing ramdomly generated data matrix

get_stats *get_stats*

Description

Calculate statistics of the given data for XINA network analysis

Usage

```
get_stats(centrality_results, na.rm = FALSE)
```

Arguments

centrality_results	Network centrality score data frame calculated by XINA network module
na.rm	If it is FALSE, no exclusion of NA values.

Value

A data frame containing statistics of XINA network centrality scores

get_theme_blank *get_theme_blank*

Description

Predefined ggplot theme for removing ticks, titles and labels of X and Y axis

Usage

```
get_theme_blank()
```

Value

A ggplot theme

get_unknown_ppi_nodes *get_unknown_ppi_nodes*

Description

Get proteins with no known interactions within the cluster based on the used protein-protein interaction database source

Usage

```
get_unknown_ppi_nodes(xina_result, cl)
```

Arguments

xina_result	A list containing XINA network analysis results. See xina_analysis
cl	the clustering number of XINA clustering results. See xina_clustering

Value

A data frame containing proteins with no known interactions within the cluster based on the used protein-protein interaction database source

Examples

```
# load XINA example data
data(xina_example)

# load the previously processed XINA analysis results
# if you want to learn how to run 'xina_analysis', please see \link[XINA]{xina_analysis}
data(xina_result_example)

# Extract unknown PPI nodes in the cluster #1
get_unknown_ppi_nodes(xina_result_example, 1)
```

gn *A character vector containing 19,396 human genes This is for the randome data generation of XINA*

Description

- Characters of human genes

Format

A character vector containing 19,396 human genes

Source

https://www.ncbi.nlm.nih.gov/gene

gn_desc *A character vector containing 19,396 human gene descriptions This is for the randome data generation of XINA*

Description

- Human gene description corresponding to 'gn' vector

Format

A character vector containing 19,396 human gene descriptions

Source

https://www.ncbi.nlm.nih.gov/gene

hprd_ppi *Protein-protein interaction resource downloaded from HPRD DB A data frame containing HRPD protein-protein interaction data*

Description

- gene_symbol_1. Gene name interacting with gene name in 'gene_symbol_2'
- gene_symbol_2. Gene name interacting with gene name in 'gene_symbol_1'
- Experiment_type. Experimental or computational methods supporting the interaction

Format

A data frame containing HRPD protein-protein interaction data

Source

http://www.hprd.org/

length2 *length2*

Description

Customized function for vector length calculation

Usage

```
length2(x, na.rm = FALSE)
```

Arguments

x	A vector
na.rm	If it is FALSE, no exclusion of NA values.

Value

A vector length

---

load_previous_results *load_previous_results*

Description

Get previous XINA clustering results to R space

Usage

```
load_previous_results(clustering_dir = getwd(), data_column = NULL,
  fp_clusters = "xina_clusters.csv")
```

Arguments

clustering_dir	The directory path of XINA clustering results
data_column	A vector containing column names of data matrix
fp_clusters	File path of XINA clustering results

Value

Comma-separated file containing aligned XINA clustering results.

Examples

```
# Load XINA's example data
data(xina_example)
write.csv(example_clusters$aligned,"xina_clusters_aligned.csv")
write.csv(example_clusters$clusters,"xina_clusters.csv")

# Reload the clustering result
example_clusters_reloaded <- load_previous_results(".")
```

make_random_xina_data *make_random_xina_data*

Description

Generate random proteomics dataset for testing XINA 'make_random_xina_data' will make random proteomics data for XINA test. The generated data will have three conditions and seven time points, c("0hr", "2hr", "6hr", "12hr", "24hr", "48hr", "72hr").

Usage

```
make_random_xina_data(n = 500, mtor = TRUE, time_points = c("0hr",
  "2hr", "6hr", "12hr", "24hr", "48hr", "72hr"),
  conditions = c("Control", "Stimulus1", "Stimulus2"))
```

Arguments

n	The number of proteins for one condition. Default is 500.
mtor	If it is TRUE (default), mTOR pathway genes will be significant. If it is FALSE, randomly selected genes will be significant in first three conditions.
time_points	A vector containing time points of the data matrix
conditions	A vector containing condition information, for example normal, disease and drug treated disase.

Value

Three comma-separated files containing time-series data for XINA

Examples

```
make_random_xina_data()
g1 <- read.csv("Control.csv", check.names=FALSE,
stringsAsFactors = FALSE)
g2 <- read.csv("Stimulus1.csv", check.names=FALSE,
stringsAsFactors = FALSE)
g3 <- read.csv("Stimulus2.csv", check.names=FALSE,
stringsAsFactors = FALSE)

head(g1)
head(g2)
head(g3)
```

mutate_colors *mutate_colors*

Description

'mutate_colors' generates new color scheme for XINA clustering plot based on condition composition results (plot_condition_compositions). If any clusters have higher percentage than the 'threshold_percent', XINA will assign new colors in accordance to 'color_for_condition'. If not, XINA will give 'gray' color or user-defined color via 'null_color' parameter.

Usage

```
mutate_colors(condition_composition, color_for_condition,
  null_color = "gray", threshold_percent = 50)
```

Arguments

condition_composition	A data frame generated by plot_condition_compositions
color_for_condition	A vector like 'color_for_condition' of xina_clustering
null_color	Default is 'gray'. This color is for clusters that are not biased to any of experimental conditions
threshold_percent	Default is 50. The percentage threshold for giving new colors

Value

A data frame containing statistics of XINA network centrality scores

Examples

```
# load XINA example data
data(xina_example)

# Plot condition composition pie-chart with default option
condition_composition <- plot_condition_compositions(example_clusters)
example_clusters$color_for_clusters <- mutate_colors(condition_composition,
example_clusters$color_for_condition)
plot_clusters(example_clusters, xval=c(0,2,6,12,24,48,72), xylab=FALSE)
```

`organize_clusters` *organize_clusters*

Description

Organize XINA clustering information by gene name

Usage

```
organize_clusters(clustering_dir = getwd(), super_ds, file_out = TRUE)
```

Arguments

`clustering_dir`	The directory path of XINA clustering results
`super_ds`	XINA clusters
`file_out`	If it is TRUE, it writes the aligned clustering informaion to "xina_clusters_aligned.csv" file.

Value

Comma-separated file containing aligned XINA clustering results.

`plot_clusters` *plot_clusters*

Description

Draw all the clustering results. 'plot_clusters' draws two plots, scaled and unscaled line graphs. Scaled graphs have same y limits that are 0 to 1 by default, but can be changed via 'y_lim' parameter.

Usage

```
plot_clusters(clustering_result, y_lim = NULL, xval = NULL,
  xtickmark = NULL, xylab = TRUE, ggplot_theme = NULL)
```

Arguments

`clustering_result`	A list containing XINA clustering results. See xina_clustering
`y_lim`	Y axis limit. If you set y_lim=c(0,1), 'plot_clusters' will plot line graphs scaled from 0 to 1 in y-axis Default is NULL, which means unscaled line graphs.
`xval`	XINA basically considers time points as a ordinary variable, like 1,2,3,4...n. You can make the time points as a continuous variable using xval.
`xtickmark`	Change X axis tick marks. Default is data_column of the clustering result list.
`xylab`	If it is FALSE, x and y labels will be blank. If it is TRUE (defualt), x and y labels will be shown.
`ggplot_theme`	This is ggplot theme to modify XINA clustering plot.

Value

Line graphs of all the clusters

Examples

```
library(ggplot2)

# load XINA example data
data(xina_example)

# Draw clustering plots
plot_clusters(example_clusters)

# Apply theme to the clustering plot
theme1 <- theme(title=element_text(size=8, face='bold'),
axis.text.x = element_text(size=7),
axis.text.y = element_blank(),
axis.ticks.x = element_blank(),
axis.ticks.y = element_blank(),
axis.title.x = element_blank(),
axis.title.y = element_blank())
plot_clusters(example_clusters, ggplot_theme=theme1)
```

`plot_clusters_all` *plot_clusters_all*

Description

Draw line graphs of all the proteins in the given dataset

Usage

```
plot_clusters_all(clustering_result, selected_condition = NULL)
```

Arguments

`clustering_result`
: A list containing XINA clustering results. See xina_clustering

`selected_condition`
: A condition name to draw the kinetics plot

Value

a list containing clustering results and pdf file containing a BIC plot in current working directory.

Examples

```
# load XINA example data
data(xina_example)

# Plot kinetics of all the proteins in Control
plot_clusters_all(example_clusters, selected_condition="Control")
```

```
# Plot kinetics of all the proteins in Stimulus1
plot_clusters_all(example_clusters, selected_condition="Stimulus1")

# Plot kinetics of all the proteins in Stimulus2
plot_clusters_all(example_clusters, selected_condition="Stimulus2")

# Plot kinetics of all the proteins in three data
plot_clusters_all(example_clusters)
```

`plot_condition_compositions` *plot_condition_compositions*

Description

computes condition composition of the XINA clustering results and draws pie-charts.

Usage

```
plot_condition_compositions(clustering_result, bullseye = FALSE,
  ggplot_theme = NULL)
```

Arguments

`clustering_result`	A list containing XINA clustering results. See xina_clustering
`bullseye`	If it is TRUE, draw bullseye plot instead of the pie-chart. Default is FALSE
`ggplot_theme`	This is ggplot theme to modify condition composition pie-chart and bulles eye plots.

Value

A condition composition plot and a data frame containing condition compositions of the clusters

Examples

```
# load XINA example data
data(xina_example)

# Plot condition composition pie-chart with default option
plot_condition_compositions(example_clusters)

# Make a new color code for conditions
condition_colors <- c("tomato","steelblue1","gold")
names(condition_colors) <- example_clusters$condition
example_clusters$color_for_condition <- condition_colors

# Draw condition composition pie-chart with the new color code
plot_condition_compositions(example_clusters)

# Draw condition composition bullseye plot
plot_condition_compositions(example_clusters, bullseye = TRUE)
```

plot_enrichment_results *plot_enrichment_results*

Description

Plot GO and KEGG enrichment results

Usage

```
plot_enrichment_results(enriched_results,
  term_description = "term_description", sig_score = "pvalue",
  num_terms = 0, get_log = TRUE, fill_color = "darkgray")
```

Arguments

enriched_results	GO or KEGG enrichment results. See xina_enrichment and xina_enrichment
term_description	Description of terms to be drawn on Y axis. Default is "term_description" of XINA enrichment results.
sig_score	significant score to plot on X axis. Default is "pvalue".
num_terms	The number of terms to be plotted. Default is 0, which menas no limit.
get_log	If this is TRUE, 'plot_enrichment_results' will take -log10 of p-values.
fill_color	Default is 'darkgray'. You can change color of bars.

Value

ggplot bar graph

Examples

```
## Not run:
library(STRINGdb)

# load XINA example data
data(xina_example)

# Get STRING database for protein-protein intereaction information
string_db <- STRINGdb$new( version="10", species=9606,
score_threshold=0, input_directory="" )
string_db

# XINA analysis with STRING DB
xina_result <- xina_analysis(example_clusters, string_db)

# Select proteins that showed cluster #1 in the Stimulus2 condition
subgroup <- subset(example_clusters$aligned, Stimulus2==1)
protein_list <- as.vector(subgroup$`Gene name`)

# Enrichment test and get significantly enriched functional terms
# that have adjuseted p-value less than 0.1
```

```
kegg_enriched <- xina_enrichment(string_db, protein_list,
enrichment_type = "KEGG", pval_threshold=0.1)
plot_enrichment_results(kegg_enriched$KEGG, num_terms=10)

## End(Not run)
```

`plot_NA` *plot_NA*

Description

Draw NULL plot

Usage

```
plot_NA()
```

Value

a empty plot

`rank_centrality` *rank_centrality*

Description

Give ranks based on network centrality scores

Usage

```
rank_centrality(centrality_score, type, num_breaks = 5)
```

Arguments

`centrality_score`	Network centrality score matrix
`type`	Network centrality score type, such as 'Eigenvector'
`num_breaks`	The number of ranks

Value

A vector containing ranks

string_example *Protein-protein interaction resource downloaded from STRING DB for XINA's example dataset A data frame containing protein-protein interactions*

Description

- gene_symbol_1. Gene name interacting with gene name in 'gene_symbol_2'
- gene_symbol_2. Gene name interacting with gene name in 'gene_symbol_1'
- PPI_Source. Data original source

Format

A data frame containing STRING protein-protein interaction data

Source

https://string-db.org/

xina_analysis *xina_analysis*

Description

xina_analysis is to analyze protein-protein interaction(PPI) networks using STRINGdb and igraph R package. This module computes PPI networks within each XINA clusters.

Usage

```
xina_analysis(clustering_result, ppi_db, is_stringdb = TRUE,
  flag_simplify = TRUE, node_shape = "sphere",
  num_clusters_in_row = 5, img_size = NULL, img_qual = 300)
```

Arguments

clustering_result	A list containing XINA clustering results. See xina_clustering
ppi_db	STRINGdb object
is_stringdb	If it is TRUE (default), XINA will process 'ppi_db' as STRINGdb, but it is FALSE, XINA will accepts your 'ppi_db' as it is. You can make your own igraph network using customized PPI information instead of STRINGdb.
flag_simplify	If it is TRUE (default), XINA will exclude unconnected proteins
node_shape	You can choose node shape. Default is "sphere". See shapes
num_clusters_in_row	The number of clusters in a row on the XINA network plot. Default is 5.
img_size	Set the image size. For width=1000 and height=1500, it is img_size=c(1000,1500).
img_qual	Set the image resolution. Default is 300.

Value

A PNG file (XINA_Cluster_Networks.png) displaying PPI network plots of all the clusters and a list containing XINA network analysis results.

Item	Description
All_network	PPI network of all the input proteins
Sub_network	A list containing PPI networks of each clusters
Data	XINA clustering results. See xina_clustering
Nodes	A list of proteins in each cluster
Conditions	A list of experimental condition of proteins in each cluster
Titles	A list of plot titles for XINA plotting
out_dir	A directory path storing XINA network analysis results
is_stringdb	False = different PPI DB and TRUE = STRING DB

Examples

```
## Not run:
# load XINA example data
data(xina_example)

# use the following code for utilizing up-to-date STRING DB
tax_id <- 9606  # for human
# tax_id <- 10090  # for mouse
library(STRINGdb)
library(igraph)
string_db <- STRINGdb$new( version='10', species=tax_id, score_threshold=0, input_directory='' )
string_db
xina_result <- xina_analysis(example_clusters, string_db, flag_simplify=FALSE)

# Run XINA with a protein-protein interaction edgelist
data(HPRD)
net_all <- simplify(graph_from_data_frame(d=hprd_ppi, directed=FALSE),
remove.multiple = FALSE, remove.loops = TRUE)
xina_result <- xina_analysis(example_clusters, net_all, is_stringdb=FALSE, flag_simplify=FALSE)

## End(Not run)
```

`xina_clustering` *xina_clustering*

Description

Clustering multiplexed time-series omics data to find co-abundance profiles

Usage

```
xina_clustering(f_names, data_column, out_dir = getwd(),
  nClusters = 20, norm = "sum_normalization", chosen_model = "")
```

Arguments

f_names	A vector containing input file (.csv) paths
data_column	A vector containing column names (1st row of the input file) of data matrix
out_dir	A directory path for saving clustering results. (default: out_dir=getwd())
nClusters	The number of desired maximum clusters
norm	Default is "sum_normalization". Sum-normalization is to divide the data matrix by row sum. If you want to know more about sum-normalization, see https://www.ncbi.nlm.nih.gov/pubmed/19861354. "zscore" is to calculate Z score for each protein. See scale.
chosen_model	You can choose a specific model rather than testing all the models that are available in mclust. mclustModelNames If you want k-means clustering instead of the model-based clustering, use "kmeans" here.

Value

a plot containing a BIC plot in current working directory and a list containing below information:

Item	Description
clusters	XINA clustering results
aligned	XINA clustering results aligned by ID
data_column	Data matrix column names
out_dir	The directory path containing XINA results
nClusters	The number of clusters desired by user
max_cluster	The number of clusters optimized by BIC
chosen_model	The used covariance model for model-based clustering
optimal_BIC	BIC of the optimized covariance model
condition	Experimental conditions of the user input data
color_for_condition	Colors assigned to each experimental conditions which is used for condition composition plot
color_for_clusters	Colors assigned to each clusters which is used for XINA clustering plot
norm_method	Used normalization method

Examples

```
# Generate random multiplexed time-series data
random_data_info <- make_random_xina_data()

# Data files
data_files <- paste(random_data_info$conditions, ".csv", sep='')

# time points of the data matrix
data_column <- random_data_info$time_points

# mclust requires the fixed random seed to get reproduce the clustering results
set.seed(0)

# Run the model-based clustering to find co-abundance profiles
example_clusters <- xina_clustering(data_files, data_column=data_column,
nClusters=30)

# Run k-means clustering to find co-abundance profiles
example_clusters <- xina_clustering(data_files, data_column=data_column,
```

```
nClusters=30,
chosen_model="kmeans")
```

`xina_enrichment` *xina_enrichment*

Description

xina_enrichment conducts functional enrichment tests using gene ontology or KEGG pathway terms for a given protein list

Usage

```
xina_enrichment(string_db, protein_list, enrichment_type = "GO",
  pval_threshold = 0.05, methodMT = "fdr")
```

Arguments

`string_db`	STRINGdb object
`protein_list`	A vector of gene names to draw protein-protein interaction network.
`enrichment_type`	A functional annotation for the enrichment test. 'enrichment_type' should be one of 'GO' and 'KEGG',
`pval_threshold`	P-value threshold to get significantly enriched terms from the given proteins
`methodMT`	Method for p-value adjustment. See get_enrichment. Default is 'fdr'.

Value

A list of data frames containing enrichment results

Examples

```
## Not run:
library(STRINGdb)
library(Biobase)

# load XINA example data
data(xina_example)

# Get STRING database for protein-protein intereaction information
string_db <- STRINGdb$new( version="10", species=9606, score_threshold=0, input_directory="" )
string_db

# XINA analysis with STRING DB
xina_result <- xina_analysis(example_clusters, string_db)

# Select proteins that showed cluster #1 in the Stimulus2 condition
subgroup <- subset(example_clusters$aligned, Stimulus2==1)
protein_list <- as.vector(subgroup$`Gene name`)

# Enrichment test using KEGG pathway terms that have adjuseted p-value less than 0.1
```

```
kegg_enriched <- xina_enrichment(string_db, protein_list,
enrichment_type = "KEGG", pval_threshold=0.1)
plot_enrichment_results(kegg_enriched$KEGG, num_terms=10)

# Enrichment test using GO terms that have adjuseted p-value less than 0.1
go_enriched <- xina_enrichment(string_db, protein_list,
enrichment_type = "GO", pval_threshold=0.1)
plot_enrichment_results(go_enriched$Component, num_terms=10)

## End(Not run)
```

`xina_plot_all` *xina_plot_all*

Description

xina_plot_all is to draw protein-protein interaction network plots of all the clusters

Usage

```
xina_plot_all(xina_result, clustering_result, condition = "all",
  centrality_type = NULL, flag_simplify = TRUE, num_breaks = 5,
  layout_specified = "", vertex_label_flag = FALSE,
  vertex.label.color = "black", vertex.color = "", edge.color = NULL,
  vertex.label.dist = 0.6, vertex.label.cex = 0.8,
  edge.arrow.size = 0.4, vertex.size = 10, vertex.shape = "sphere",
  legend_location = "bottom", num_clusters_in_row = 5,
  flag_unknown_only = FALSE, img_size = NULL, img_qual = 300)
```

Arguments

`xina_result` A list containing XINA network analysis results. See xina_analysis

`clustering_result`
A list containing XINA clustering results. See xina_clustering

`condition` Default is 'all', which means use all the proteins to draw graphs. If you specify the experimental condition name used for XINA clustering, xina_plot_all will draw graphs using specific condition's proteins.

`centrality_type`
'centrality_type' should be one of c('Degree', 'Eigenvector', 'Hub', 'Authority', 'Closeness', 'Betweenness')

Centrality score	igraph function
Degree	degree
Eigenvector	eigen_centrality
Hub	hub_score
Authority	authority_score
Closeness	closeness
Betweenness	betweenness

`flag_simplify` If it is TRUE (default), XINA will exclude unconnected proteins

`num_breaks` 'num_breaks' is the number of ranks based on network centrality. Default is 5.

`layout_specified`
This can change network layout. 'layout_specified' should be one of c('sphere', 'star', 'gem', 'tree', 'circle', 'random', 'nicely'). XINA's layouts are based on igraph's layout. See layout_

Layout	igraph layout name
sphere	layout_on_sphere
star	layout_as_star
gem	layout_with_gem
tree	layout_as_tree
circle	layout_in_circle
random	layout_randomly
nicely	layout_nicely

Default is 'layout_nicely' of igraph

`vertex_label_flag`
If vertex_label_flag is TRUE (default), igraph network graphs will be labeled by gene names If vertex_label_flag is FALSE, igraph network graphs will be drawn without labels

`vertex.label.color`
Color of labels. Default is black

`vertex.color` Color of nodes. Default is pink.

`edge.color` Color of edges. Default is pink.

`vertex.label.dist`
Distance between node and label. Default is 0.6

`vertex.label.cex`
Size of labels Default is 0.8

`edge.arrow.size`
Size of edges Default is 0.4

`vertex.size` Size of nodes Default is 10

`vertex.shape` You can choose node shape. Default is 'sphere'. See shapes

`legend_location`
If centrality_type is chosen, xina_plot_single add the color legend guiding rank of nodes based on the centrality score. Default is 'bottomright', but you can choose one of these 'bottomright', 'bottom', 'bottomleft', 'left', 'topleft', 'top', 'topright', 'right' and 'center'.

`num_clusters_in_row`
The number of clusters in a row on the XINA network plot. Default is 5.

`flag_unknown_only`
If this is TRUE, 'xina_plot_all' will plot proteins that do not have any protein-protein interaction in the given database

`img_size` Set the image size. For width=1000 and height=1500, it is img_size=c(1000,1500). Default is c(3000,3000)

`img_qual` Set the image resolution. Default is 300.

Value

PNG images of PPI network plots of all the clusters

Examples

```
## the following code is to show how it works quickly
## load XINA example data
data(xina_example)

## load the previously processed XINA analysis results
# if you want to learn how to run 'xina_analysis', please see \link[XINA]{xina_analysis}
data(xina_result_example)

# XINA network plots
xina_plot_all(xina_result_example, example_clusters)

# XINA network plots for Control condition
xina_plot_all(xina_result_example, example_clusters, condition='Control')
```

`xina_plot_bycluster` *xina_plot_bycluster*

Description

xina_plot_bycluster is to draw protein-protein interaction network plots of each cluster

Usage

```
xina_plot_bycluster(xina_result, clustering_result, cl = NULL,
  condition = "all", flag_legend = TRUE, centrality_type = NULL,
  flag_simplify = TRUE, layout_specified = "",
  vertex_label_flag = TRUE, vertex.label.dist = 0.6,
  vertex.label.cex = 0.8, edge.arrow.size = 0.4, vertex.size = 10,
  vertex.shape = "sphere", vertex.color = "",
  edge.color = "darkgray", legend_location = "bottom",
  flag_unknown_only = FALSE)
```

Arguments

`xina_result`	A list containing XINA network analysis results. See xina_analysis
`clustering_result`	A list containing XINA clustering results. See xina_clustering
`cl`	Cluster number in the XINA clustering results
`condition`	Default is 'all', which means use all the proteins to draw graphs. If you specify the experimental condition name used for XINA clustering,
`flag_legend`	If it is TRUE, a legend will be printed out together.
`centrality_type`	'centrality_type' should be one of c('Degree', 'Eigenvector', 'Hub', 'Authority', 'Closeness', 'Betweenness')

Centrality score	igraph function
Degree	degree
Eigenvector	eigen_centrality

Hub	hub_score
Authority	authority_score
Closeness	closeness
Betweenness	betweenness

`flag_simplify` If it is TRUE (default), XINA will exclude unconnected proteins

`layout_specified`
This can change network layout. 'layout_specified' should be one of c('sphere', 'star', 'gem', 'tree', 'circle', 'random', 'nicely'). XINA's layouts are based on igraph's layout. See layout_

Layout	igraph layout name
sphere	layout_on_sphere
star	layout_as_star
gem	layout_with_gem
tree	layout_as_tree
circle	layout_in_circle
random	layout_randomly
nicely	layout_nicely

Default is 'layout_nicely' of igraph

`vertex_label_flag`
If vertex_label_flag is TRUE (default), igraph network graphs will be labeled by gene names If vertex_label_flag is FALSE, igraph network graphs will be drawn without labels

`vertex.label.dist`
Distance between node and label. Default is 0.6

`vertex.label.cex`
Size of labels Default is 0.8

`edge.arrow.size`
Size of edges Default is 0.4

`vertex.size` Size of nodes Default is 10

`vertex.shape` You can choose node shape. Default is 'sphere'. See shapes

`vertex.color` Color of nodes. Default is pink.

`edge.color` Color of edges. Default is pink.

`legend_location`
If centrality_type is chosen, xina_plot_single add the color legend guiding rank of nodes based on the centrality score. Default is 'bottomright', but you can choose one of these 'bottomright', 'bottom', 'bottomleft', 'left', 'topleft', 'top', 'topright', 'right' and 'center'.

`flag_unknown_only`
If this is TRUE, 'xina_plot_bycluster' will plot proteins that do not have any protein-protein interaction in the given database

Value

A PNG file (XINA_Cluster_Networks.png) displaying protein-protein interaction network plots of all the clusters and a list containing XINA network analysis results

PNG images of PPI network plots of all the clusters

Examples

```
## the following code is to show how it works quickly
## load XINA example data
data(xina_example)

## load the previously processed XINA analysis results
# if you want to learn how to run 'xina_analysis', please see \link[XINA]{xina_analysis}
data(xina_result_example)

# plot cluster #1
xina_plot_bycluster(xina_result_example, example_clusters, cl=1)

# plot PPI network of Control condition in cluster #1
xina_plot_bycluster(xina_result_example, example_clusters, cl=1, condition='Control')
```

`xina_plot_single` *xina_plot_single*

Description

xina_plot_single draws protein-protein interaction network plot for given 'protein_list'.

Usage

```
xina_plot_single(xina_result, protein_list, centrality_type = NULL,
  layout_specified = "", vertex_label_flag = TRUE, main = NULL,
  vertex.label.color = "black", vertex.color = NA,
  edge.color = "darkgray", vertex.label.dist = 0.6,
  vertex.label.cex = 0.8, edge.arrow.size = 0.4, vertex.size = 10,
  vertex.shape = "sphere", legend_location = "bottom",
  num_breaks = 5, digits_round_up = 5, flag_simplify = TRUE,
  flag_legend = TRUE)
```

Arguments

`xina_result`	A list containing XINA network analysis results. See xina_analysis
`protein_list`	A vector of gene names to draw a protein-protein interaction network graph.
`centrality_type`	'centrality_type' should be one of c('Degree', 'Eigenvector', 'Hub', 'Authority', 'Closeness', 'Betweenness')

Centrality score	igraph function
Degree	degree
Eigenvector	eigen_centrality
Hub	hub_score
Authority	authority_score
Closeness	closeness
Betweenness	betweenness

`layout_specified`
: This can change network layout. 'layout_specified' should be one of c('sphere', 'star', 'gem', 'tree', 'circle', 'random', 'nicely'). XINA's layouts are based on igraph's layout. See layout_

Layout	igraph layout name
sphere	layout_on_sphere
star	layout_as_star
gem	layout_with_gem
tree	layout_as_tree
circle	layout_in_circle
random	layout_randomly
nicely	layout_nicely

Default is 'layout_nicely' of igraph

`vertex_label_flag`
: If vertex_label_flag is TRUE (default), igraph network graphs will be labeled by gene names If vertex_label_flag is FALSE, igraph network graphs will be drawn without labels

`main`
: Title of network figure. IF it is NULL (default), it will be the number of plotted proteins

`vertex.label.color`
: Color of labels. Default is black

`vertex.color`
: Color of nodes. Default is pink.

`edge.color`
: Color of edges. Default is pink.

`vertex.label.dist`
: Distance between node and label. Default is 0.6

`vertex.label.cex`
: Size of labels Default is 0.8

`edge.arrow.size`
: Size of edges Default is 0.4

`vertex.size`
: Size of nodes Default is 10

`vertex.shape`
: You can choose node shape. Default is 'sphere'. See shapes

`legend_location`
: If centrality_type is chosen, 'xina_plot_single' adds the color legend guiding rank of nodes based on the centrality score. Default is 'bottomright', but you can choose one of these 'bottomright', 'bottom', 'bottomleft', 'left', 'topleft', 'top', 'topright', 'right' and 'center'.

`num_breaks`
: 'num_breaks' is the number of ranks based on network centrality. Default is 5.

`digits_round_up`
: See Round

`flag_simplify`
: If it is TRUE (default), XINA will exclude unconnected proteins

`flag_legend`
: If it is TRUE, a legend will be printed out together.

Value

A PNG file (XINA_Cluster_Networks.png) displaying protein-protein interaction network plots of all the clusters and a list containing XINA network analysis results

Examples

```
## the following code is to show how it works quickly
## load XINA example data
data(xina_example)

## load the previously processed XINA analysis results
# if you want to learn how to run 'xina_analysis', please see \link[XINA]{xina_analysis}
data(xina_result_example)

# get gene names that are clustered to #21 in "Stimulus2" condition
subgroup <- subset(example_clusters$aligned, Stimulus2==21)
protein_list <- subgroup$`Gene name`

# Calculate protein-protein interaction network
xina_plot_single(xina_result_example, protein_list)

# Calculate protein-protein interaction network and Eigenvector centrality
eigen_info <- xina_plot_single(xina_result_example, protein_list, centrality_type='Eigenvector')
```

`xina_result_example` *Previously processed xina analysis using XINA's random example data*
A list containing 'xina_analysis' results

Description

- All_network. PPI network of all the input proteins
- Sub_network. A list containing PPI networks of each clusters
- Data. XINA clustering results. See xina_clustering
- Nodes. A list of proteins in each cluster
- Conditions. A list of experimental condition of proteins in each cluster
- Titles. A list of plot titles for XINA plotting
- out_dir. A directory path storing XINA network analysis results
- is_stringdb. False = different PPI DB and TRUE = STRING DB

Format

A data frame containing STRING protein-protein interaction data

Source

XINA

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