Package 'TrendCatcher'

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R topics documented:
cal_p

2 cal_p

	draw_GOHeatmap	6
	draw_TimeHeatmap_enrichR	7
	draw_TimeHeatmap_GO	9
	draw_TrajClusterGrid	10
	draw_TrajClusterPie	11
	fit_single_gene_const	12
	fit_single_gene_spline	12
	get_GeneEnsembl2Symbol	13
	get_rep_array	13
	get_Symbol2GeneEnsembl	14
	get_time_array	14
	preprocess_TrendCatcher	
	run_TrendCatcher	
	transform_single_gene_df	17
Index		19
cal_p	Calculate the significance of the dynamic signal for a single gene's single time expression. Compared to baseline NB confidence interval.	

Description

Calculate the significance of the dynamic signal for a single gene's single time expression. Compared to baseline NB confidence interval.

Usage

```
cal_p(obs.val, size, mu)
```

Arguments

obs.val, estimated value from non-baseline model.

size, the size of negative binomial model.

mu, the estimated mean of constant negative binomial model

Value

a numeric p-value for time t.

```
cal_time_p_single_gene
```

Calculate the significance of the dynamic signal for a single gene's over all the time points.

Description

Calculate the significance of the dynamic signal for a single gene's over all the time points.

Usage

```
cal_time_p_single_gene(const.output, spline.output)
```

Arguments

Value

p-value for a single point.

```
Check_CountTable_Format
```

Check the Input Count Table Format

Description

This function takes the CSV file path of the count table provided by user. The input count table must be a CSV file, includes integer count table, first column are the GENE SYMBOL or GENE ENSEMBL, and first row are SAMPLE NAME. The count table is a rounded up after normalization and batch correction. Please check TrendCatcher QC functions for normalization and batch correction details. The row names must be in the format of "ProjectName_Time_Rep1" format. ProjectName is a string, can be single letter. Time is a integer. Rep is the replicate ID. This function checked the count table format, and order the sample columns based on its time order. It will return a right formatted count table to run TrendCatcher.

Usage

```
Check_CountTable_Format(count.table.path, min.low.count = 1)
```

Arguments

```
count.table.path,
string contain the absolute path of the CSV file count table, with first column as
GENE SYMBOL or GENE ENSEMBL and first row as SAMPLE NAME (with
format composed by project name, time and replicateID, such as "Lung_0_Rep1")
min.low.count,
one numeric variable, the minimal count threshold for filtering low count within
each time group. By default it is 1.
```

Value

A list object, contains "raw.df", original count table ordered by time and replicate ID; "count.table", filtered out low genes for further fitting; "removed.genes", low count genes.

Examples

```
example.file.path<-system.file("extdata", "Lung_DemoCountTable.csv", package = "TrendCatcher")
## Not run:
count<-Check_CountTable_Format(example.file.path, min.low.count = 1)
## End(Not run)</pre>
```

combine_p_single_gene Combine multiple p-value using Fisher's p-value combination method.

Description

Combine multiple p-value using Fisher's p-value combination method.

Usage

```
combine_p_single_gene(p.arr)
```

Arguments

```
p.arr, a vector of p-values.
```

Value

a numeric combined p-value.

draw_GeneTraj 5

draw_GeneTraj

Draw gene(s) trajectory with observed data and fitted data

Description

This function takes the master.list object output from run_TrendCatcher function, and an array of gene(s). It will draw gene(s) trajectory with observed data and fitted data.

Usage

```
draw_GeneTraj(
  master.list,
  gene.symbol.arr,
  savepdf.path = NA,
  ncol = 5,
  nrow = 3,
  fig.width = 15,
  fig.height = 10
)
```

Arguments

```
master.list,
                  the list object returned from run_TrendCatcher.
gene.symbol.arr,
                  a character array. It must be a subset of row names from the master.list$master.table$Symbol.
                  The Symbol column need get_GeneEnsembl2Symbol function to convert origi-
                  nal ensembl ID into gene symbol.
savepdf.path,
                  an obsolute file path to save the figure as PDF file. By default is NA, it will be
                  an integer variable. If more than one gene need to be plotted, it will layout as
ncol,
                  grid structure. This represents the number of column of the grid layout.
                  an integer variable. If more than one gene need to be plotted, it will layout as
nrow,
                   grid structure. This represents the number of row of the grid layout.
fig.width,
                   a numeric variable. If save figure as PDF file, the width of the PDF file. By
                   default is 15.
fig.height,
                  a numeric variable. If save figure as PDF file, the height of the PDF file. By
                   default is 10.
master.list.new,
                  a list object. Output from the run_TrendCatcher with ID conversion to add Sym-
                  bol column to master table.
count.table,
                  the count table of mRNA.
gene.name,
                  name of the gene you would like to plot.
```

Value

"arrangelist" "list" object.

6 draw_GOHeatmap

Examples

```
gene.symbol.arr <- c("Cxcl1", "Cxcl5", "Cxcl10", "Cxcl11", "Abcb1b", "Icam1", "Ifitm1", "Ifitm2", "Ifitm3")
example.file.path<-system.file("extdata", "BrainMasterList.rda", package = "TrendCatcher")
load(file= example.file.path)
gene.symbol.df<-get_GeneEnsembl2Symbol(ensemble.arr = master.list$master.table$Gene)
master.table.new<-cbind(master.list$master.table, gene.symbol.df[match(master.list$master.table$Gene, gene.symbol.arr, savepdf.path = NA, ncol = 3, nrow = 3, fig.width =15, fig.heigl</pre>
```

draw_GOHeatmap

Draw GOHeatmap contianing Terms from TimeHeatmap and included Genes

Description

This funcitons takes the master.list output from run_TrendCatcher, and merge.df output from draw_TimeHeatmap_GO and draw_TimeHeatmap_enrichR. And showing all the genes used for enrichment analysis and their logFC compared to previous break point.

Usage

```
draw_GOHeatmap(
  master.list,
  time.window = "",
  go.terms = "",
  id.ensembl = TRUE,
  merge.df = NA,
  logFC.thres = 2,
  save.as.PDF = FALSE,
  pdf.width = 7,
  pdf.height = 15
)
```

Arguments

a list object. The output from run_TrendCatcher function, contains master.table master.list, element. a character array. Must be an array of go terms from the merge.df\$Description. go.terms, a logic variable. If using ensembl as the keytype. This must match the row name id.ensembl, of master.table. By default is TRUE. a dataframe. The output dataframe from output list of draw_TimeHeatmap_GO merge.df, or draw_TimeHeatmap_enrichR. Use \$merge.df to obtain it. logFC.thres, a numeric variable. The logFC threshold compared to each genes previous break point expression level. By default is 2, meaning for each gene, the current time window's expression level is 2-fold compared to previous break point's expression level.

```
a character variable. If need to save the figure into PDF file. This must be an absolute file path. If not needed save as PDF file, set it to NA. By default iS NA. pdf.width, a numeric variable. The width of PDF file. By default is 13. pdf.height, a numeric variable. The height of PDF file. By default is 15. time.windown, a character. Must be one of the merge.df$t.name.
```

A list object, including elements names merge.df and time.heatmap. time.heatmap is the ggplot object. merge.df includes all the enrichR enrichment result and activation/deactivation time.

Examples

```
## Not run:
example.file.path<-system.file("extdata", "BrainMasterList.rda", package = "TrendCatcher")
load(example.file.path)
th.obj<-draw_TimeHeatmap_GO(master.list = master.list)
merge.df<-th.obj$merg.df

time.window<-"0h-6h"
go.terms<-c("regulation of defense response", "leukocyte migration", "myeloid leukocyte migration", "leukocyte che"
granulocyte chemotaxis", "cellular response to chemokine", "chemokine-mediated signaling pathway", "angiogenesis
go.df<-draw_GOHeatmap(master.list = master.list, time.window = "0h-6h", go.terms = go.terms, id.ensembl = TRUE, me
## End(Not run)</pre>
```

draw_TimeHeatmap_enrichR

Draw Time-Heatmap Using enrichR

Description

This funcitons takes the master.list output from run_TrendCatcher. And apply a time window sliding strategy to capture all the genes increased/decreased compared to its previous break point, and apply enrichR enrichment analysis.

Usage

```
draw_TimeHeatmap_enrichR(
  master.list,
  logFC.thres = 1,
  top.n = 10,
  dyn.gene.p.thres = 0.05,
  dbs = "BioPlanet_2019",
  id.ensembl = TRUE,
  term.width = 80,
  OrgDb = "org.Mm.eg.db",
```

```
GO.enrich.p = 0.05,
figure.title = "",
save.pdf.path = NA,
pdf.width = 13,
pdf.height = 15
```

Arguments

master.list, a list object. The output from run_TrendCatcher function, contains master.table element. logFC.thres, a numeric variable. The logFC threshold compared to each genes previous break point expression level. By default is 1, meaning for each gene, the current time window's expression level is 2-fold compared to previous break point's expression level. an integer variable. The top N GO enrichment term need to be shown in the top.n, Time-Heatmap for up and down regulated pathway. By default is 10. Top 20 GO terms, 10 from up-regulated pathway and 10 from down-regulated pathway will shown in Time-Heatmap. dyn.gene.p.thres, a numeric variable. The DDEGs dynamic p-value threshold. By default is 0.05. dbs, must one of the enrichR supported database name. To check the list, run dbs <listEnrichrDbs() command. By default is "BioPlanet_2019". id.ensembl, a logic variable. If using ensembl as the keytype. This must match the row name of master.table. By default is TRUE. an integer variable. The character length for each GO term. If one GO term term.width, is super long, we can wrap it into term.width of strings into multiple rows. By default if 80. GO.enrich.p, an numeric variable. The GO enrichment p-value threshold. By default if 0.05. figure.title, a character variable. The main title of Time-Heatmap. save.pdf.path, a character variable. If need to save the figure into PDF file. This must be an absolute file path. If not needed save as PDF file, set it to NA. By defualt iS NA. pdf.width, a numeric variable. The width of PDF file. By default is 13.

Value

pdf.height,

is "BP".

ont,

A list object, including elements names merge.df and time.heatmap. time.heatmap is the ggplot object. merge.df includes all the enrichR enrichment result and activation/deactivation time.

a numeric variable. The height of PDF file. By default is 15.

one of "BP", "MF", and "CC" subontologies, or "ALL" for all three. By default

Examples

```
## Not run:
example.file.path<-system.file("extdata", "BrainMasterList.rda", package = "TrendCatcher")
load(example.file.path)
th.obj<-draw_TimeHeatmap_enrichR(master.list = master.list)
print(th.obj$time.heatmap)
head(th.obj$merge.df)
## End(Not run)</pre>
```

draw_TimeHeatmap_GO

Draw Time-Heatmap Using Gene Ontology (GO) Enrichment

Description

This funcitons takes the master.list output from run_TrendCatcher. And apply a time window sliding strategy to capture all the genes increased/decreased compared to its previous break point, and apply GO enrichment analysis.

Usage

```
draw_TimeHeatmap_GO(
  master.list,
  logFC.thres = 1,
  top.n = 10,
  dyn.gene.p.thres = 0.05,
  keyType = "ENSEMBL",
  OrgDb = "org.Mm.eg.db",
  ont = "BP",
  term.width = 80,
  GO.enrich.p = 0.05,
  figure.title = "",
  save.pdf.path = NA,
  pdf.width = 15,
  pdf.height = 15
)
```

Arguments

master.list, a list object. The output from run_TrendCatcher function, contains master.table

logFC.thres,

a numeric variable. The logFC threshold compared to each genes previous break point expression level. By default is 1, meaning for each gene, the current time window's expression level is 2-fold compared to previous break point's expression level.

an integer variable. The top N GO enrichment term need to be shown in the top.n, Time-Heatmap for up and down regulated pathway. By default is 10. Top 20 GO terms, 10 from up-regulated pathway and 10 from down-regulated pathway will shown in Time-Heatmap. dyn.gene.p.thres, a numeric variable. The DDEGs dynamic p-value threshold. By default is 0.05. must be either ENSEMBL or SYMBOL. The row names of your master.list\$master.table. keyType, OrgDb, must be either "org.Mm.eg.db" or "org.Hg.eg.db". Currently only support mouse and human GO annotation database. one of "BP", "MF", and "CC" subontologies, or "ALL" for all three. By default ont, is "BP". an integer variable. The character length for each GO term. If one GO term term.width, is super long, we can wrap it into term. width of strings into multiple rows. By default if 80. GO.enrich.p. an numeric variable. The GO enrichment p-value threshold. By default if 0.05. a character variable. The main title of Time-Heatmap. figure.title, save.pdf.path, a character variable. If need to save the figure into PDF file. This must be an absolute file path. If not needed save as PDF file, set it to NA. By defualt iS NA. a numeric variable. The width of PDF file. By default is 15. pdf.width,

Value

pdf.height,

A list object, including elements names merge.df and time.heatmap. time.heatmap is the ggplot object. merge.df includes all the GO enrichment result and activation/deactivation time.

a numeric variable. The height of PDF file. By default is 15.

Examples

```
## Not run:
example.file.path<-system.file("extdata", "BrainMasterList.rda", package = "TrendCatcher")
load(example.file.path)
th.obj<-draw_TimeHeatmap_GO(master.list = master.list)
print(th.obj$time.heatmap)
head(th.obj$merge.df)
## End(Not run)</pre>
```

draw_TrajClusterGrid Draw Grouped DDEGs Trajectories in Grid Plot

Description

Group all DDEGs based on their sub-type trajectory patterns and plot their trajectories together, then layout all sub-type trajectory patterns which contains more than N genes in a grid plot. Each individual sub-grid plot is titled with sub-type trajectory pattern and number of genes included. X-axis is the time, Y-aixs is log2 transformed fitted count trajectory.

draw_TrajClusterPie 11

Usage

```
draw_TrajClusterGrid(
  master.list,
  min.traj.n = 10,
  save.as.PDF = NA,
  pdf.width = 10,
  pdf.height = 10
)
```

Arguments

```
master.list, a list object. The output from run_TrendCatcher function, contains master.table element.

min.traj.n, an integer variable. The minimum number of genes from the same sub-type trajectory. By default if 10.

save.as.PDF, a string. The absolute file path to save the figure as PDF file if needed. If set to NA, will print the figure instead of saving it as PDF file.

pdf.width, a numeric variable. The PDF file width size. By default is 10.

pdf.height, a numeric variable. The PDF file height size. By default is 10.
```

Description

Group all DDEGs based on their main-type and sub-type trajectory patterns and plot their composition in a hierarchical pie chart. Inner pie chart represents the main-type trajectory pattern composition. The outer pie chart represents sub-type trajectory pattern composition.

Usage

```
draw_TrajClusterPie(
  master.list,
  fig.title = "",
  inner.radius = 0.7,
  cex.out = 1,
  cex.in = 1
)
```

```
master.list, a list object. The output from run_TrendCatcher function, contains master.table element.

fig.title, a string. The main title of the figure. By default if "".
```

```
inner.radius, a numeric variable. The inner pie chart radius size. By default is 0.7.

cex.out, a numeric variable. The text size of label of outer pie chart. By default is 1.

cex.in, a numeric variable. The text size of the label of inner pie chart. By default is 1.
```

fit_single_gene_const Fit the baseline count data into a constant negative binomial model.

Description

Fit the baseline count data into a constant negative binomial model.

Usage

```
fit_single_gene_const(
  count.arr,
  disp.var,
  MAXIT = 1000,
  RELTOL = 10^(-8),
  trace = 10
)
```

Arguments

```
count.arr, a data frame returned from transform_single_gene_df, only with the baseline time.

disp.var, the dispersion value estimated from DESeq2.
```

Value

a list contain all the estimated value from NB model.

```
fit_single_gene_spline
```

Fit the non-baseline count data into a smoothed ANOVA model.

Description

Fit the non-baseline count data into a smoothed ANOVA model.

Usage

```
fit_single_gene_spline(data.trans)
```

```
data.trans, a data frame returned from transform_single_gene_df, without the baseline time.
```

a dataframe with all the fitted count from spline model.

```
get_GeneEnsembl2Symbol
```

ID convention (from ENSEMBL to SYMBOL)

Description

This function takes an array of ENSEMBL ID and convert it into GENE SYMBOL.

Usage

```
get_GeneEnsembl2Symbol(ensemble.arr, dataset = "mmusculus_gene_ensembl")
```

Arguments

```
ensemble.arr, a character array. The ENSEMBL ID array.

dataset, must be either "mmusculus_gene_ensembl" or "hsapiens_gene_ensembl".
```

Value

A data frame contains 3 columns, "Gene", "Symbol" and "description".

```
get_rep_array
```

Get the replicate array from count table

Description

It take the count table, grep the replicate element from column name. The column name of the count table must satisfy "Prj_Time_Rep1" format.

Usage

```
get_rep_array(raw.count.df)
```

Arguments

```
raw.count.df, a count table.
```

Value

a numeric array of each sample's replicate.

14 get_time_array

```
get_Symbol2GeneEnsembl
```

ID convention (from SYMBOL to ENSEMBL)

Description

This function takes an array of SYMBOL and convert it into GENE ENSEMBL.

Usage

```
get_Symbol2GeneEnsembl(symbol.arr, dataset = "mmusculus_gene_ensembl")
```

Arguments

```
symbol.arr, a character array. The SYMBOL array.

dataset, must be either "mmusculus_gene_ensembl" or "hsapiens_gene_ensembl".
```

Value

A data frame contains 3 columns, "Gene", original ID, "Symbol" and "description".

```
get_time_array
```

Get the time array from count table

Description

It take the count table, grep the time element from column name. The column name of the count table must satisfy Prj_Time_Rep1 format.

Usage

```
get_time_array(raw.count.df)
```

Arguments

```
raw.count.df, a count table.
```

Value

a numeric array of each sample's time.

```
preprocess_TrendCatcher
```

Preprocessing for TrendCatcher

Description

This is the preprocessing function to prepare the input count table for run_TrendCatcher function. It takes the CSV file count table and logic variables to check if normalization and batch correction needed for preprocessing. It creates pdf figure report to show before and after of normalization and batch correction to assess quality control (QC).

Usage

```
preprocess_TrendCatcher(
  count.table.path = "",
  need.batch.correction = TRUE,
  need.normalization = TRUE,
  batch.arr = "",
  pdf.file.path = NA,
  pdf.width = 8,
  pdf.height = 10,
  n.low.count = 10
)
```

Arguments

```
count.table.path,
```

string contain the absolute path of the CSV file count table, with first column as GENE SYMBOL or GENE ENSEMBL and first row as SAMPLE NAME (with format composed by project name, time and replicateID, such as "Lung_0_Rep1")

need.batch.correction,

logic variable. If batch correction is needed. By default is TRUE.

need.normalization,

logic variable. If normalization is needed. By default is TRUE.

batch.arr, a numeric vector of batch number. Need to be the same length as the number of

samples.

pdf.file.path,

an absolute file path for save the QC report file. If not need, set if to NA. The

report will be printed. By default is NA.

pdf.width, a numeric variable. The PDF file width size. By default is 8.

pdf.height, a numeric variable. The PDF file height size. By default is 10.

n.low.count, a numeric variable. The minimal number to filter low count genes. By default is

10.

16 run_TrendCatcher

Value

A matrix array object.

Examples

```
example.file.path<-system.file("extdata", "Brain_DemoCountRawTable.csv", package = "TrendCatcher")
## Not run:
count.table<-preprocess_TrendCatcher(count.table.path = example.file.path,
need.batch.correction = TRUE,
need.normalization = TRUE,
batch.arr ="",
pdf.file.path = NA,
pdf.width=8, pdf.height=10,
n.low.count = 10)
## End(Not run)</pre>
```

run_TrendCatcher

Run TrendCatcher Main Algorithm

Description

This is the main function to run TrendCatcher to identify Dynamic Differential Expressed Genes (DDEGs). This function loads a rounded count matrix CSV file after the normalization and batch correction, run the core algorithmand output a list object contains all the genes dynamic information.

Usage

```
run_TrendCatcher(
  count.table.path = "~/Documents/TrendCatcher/inst/extdata/Lung_DemoCountTable.csv",
  baseline.t = 0,
  time.unit = "h",
  min.low.count = 1,
  para.core.n = NA,
  dyn.p.thres = 0.05
)
```

```
count.table.path,
string contain the absolute path of the CSV file count table, with first column as GENE SYMBOL or GENE ENSEMBL and first row as SAMPLE NAME (with format composed by project name, time and replicateID, such as "Lung_0_Rep1")
baseline.t, one numeric variable, the baseline time of the longitudinal study. By default it is 0.
time.unit, one character variaable, the time unit of longitudinal study. If choose hour, please transform all sample collecting time into hour.
```

```
min.low.count,
one numeric variable, the minimal count threshold for filtering low count within each time group. By default it is 1.

para.core.n,
one numeric variable, number of cores will be used for running TrendCatcher.
By default it is NA, which will use N-1 cores from computer.

dyn.p.thres,
one numeric variable, the threshold of p-value of the dynamic gene. By default 0.05.
```

A list object, including "time.unit", "baseline.t", "t.arr", "Project.name", "raw.df", "fitted.count" and "master.table".

Examples

```
example.file.path<-system.file("extdata", "Brain_DemoCountTable.csv", package = "TrendCatcher")
## Not run:
master.list<-run_TrendCatcher(count.table.path = example.file.path,
baseline.t = 0,
time.unit = "h",
min.low.count = 1,
para.core.n = NA,
dyn.p.thres = 0.05)</pre>
## End(Not run)
```

```
transform_single_gene_df
```

Convert a single gene's count row number into data frame with two columns.

Description

Convert a single gene's count row number into data frame with two columns.

Usage

```
transform_single_gene_df(gene.row.info, gene.name, time.arr, rep.arr)
```

a dataframe object ordered by time and replicate id.

Index

```
cal_p, 2
cal_time_p_single_gene, 3
Check_CountTable_Format, 3
combine_p_single_gene, 4
draw_GeneTraj, 5
draw_GOHeatmap, 6
draw\_TimeHeatmap\_enrichR, 7
draw_TimeHeatmap_GO, 9
{\tt draw\_TrajClusterGrid}, {\tt 10}
draw_TrajClusterPie, 11
{\tt fit\_single\_gene\_const}, {\tt 12}
fit_single_gene_spline, 12
get_GeneEnsembl2Symbol, 13
get_rep_array, 13
{\tt get\_Symbol2GeneEnsembl}, 14
get_time_array, 14
preprocess_TrendCatcher, 15
run_TrendCatcher, 16
transform_single_gene_df, 17
```