Package: BioTransition (via r-universe)

May 22, 2026

Type Package

Title Dynamic Network Biomarker Analysis for Critical Transitions

Version 2.0.0

Date 2026-01-23

Description A comprehensive toolkit for detecting critical transitions and identifying dynamic network biomarkers (DNB) in biological systems. Critical transitions, characterized by sudden shifts between distinct states, are prevalent in complex biological processes including disease progression, cellular differentiation, and developmental transitions. This package implements seven complementary DNB methodologies: (1) conventional DNB (cDNB) based on the original DNB theory (Chen et al. 2012 <doi:10.1038/srep00342>); (2) topological DNB (tDNB), a novel approach utilizing network topology and scale-free properties; (3) landscape DNB (LDNB) for quantifying state transitions (Liu et al. 2019 <doi:10.1093/nsr/nwy162>); (4) local DNB (LcDNB) leveraging protein-protein interaction networks; (5) module-based DNB (MDNB) for modular analysis (Li et al. 2022 <doi:10.1016/j.xinn.2022.100364>); (6) time-series network module biomarker (TSNMB) for temporal dynamics (Zhong et al. 2022 <doi:10.1093/jmcb/mjac052>); and (7) time-series leading edge (TSLE) analysis (Liu et al. 2020 <doi:10.1093/bioinformatics/btz758>). Core computational routines are implemented in C++ via 'Rcpp' for optimal performance. Compatible with bulk RNA-seq, single-cell RNA-seq, and spatial transcriptomics data. Includes curated protein-protein interaction networks for human and mouse from the STRING database.

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URL https://github.com/SolvingLab/BioTransition, https://zaoqu-liu.r-universe.dev/BioTransition

BugReports https://github.com/SolvingLab/BioTransition/issues

biocViews Software, StatisticalMethod, Network, SystemsBiology, GeneExpression, Transcriptomics, SingleCell, Spatial, BiomedicalInformatics, DifferentialExpression

Encoding UTF-8

ByteCompile true

LazyData true

LazyDataCompression xz

Depends R (>= 4.4.0)

Imports methods, stats, utils, future (>= 1.21.0), furrr, magrittr, purrr (>= 1.0.0), dplyr (>= 1.0.0), parallel, WGCNA, dendextend, ggplot2, Rcpp (>= 1.0.0)

LinkingTo Rcpp

Suggests testthat (>= 3.0.0), knitr, rmarkdown, BiocStyle, BiocCheck

VignetteBuilder knitr

Config/testthat/edition 3

RoxygenNote 7.3.3

Roxygen list(markdown = TRUE)

Config/pak/sysreqs cmake make libicu-dev libuv1-dev

Repository https://zaoqu-liu.r-universe.dev

Date/Publication 2026-01-22 20:15:25 UTC

RemoteUrl https://github.com/SolvingLab/BioTransition

RemoteRef HEAD

RemoteSha 9168d50e451c54ba739812a2f46a4ff5d05d9cbe

Contents

cDNB *Conventional DNB analysis*

Description

Performing conventional dynamic network biomarker analysis based on the original DNB theory proposed by Chen et al. (2012).

Usage

```
cDNB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  variation.method = "sd",
  min.size = 10,
  max.size = 2000,
  AddModuleSize = FALSE
)
```

Arguments

`expr`	A expression dataframe with gene rows and sample columns.
`state`	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
`state.levels`	A vector for state sequence.
`cor.method`	specifies the method for correlation analysis.
`p.adjust.method`	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
`variation.method`	specifies the method for calculating gene variation. sd or cv.
`min.size`	Minimum gene number of gene modules.
`max.size`	Maximum gene number of gene modules.
`AddModuleSize`	Whether to consider gene module size when calculating DNB score.

Value

A list containing:

DNB.score A data.frame with composite index (CI) values for each state, including V_in (mean variation), R_in (mean correlation within DNB), and R_out (mean correlation with non-DNB genes)

DNB.genes Character vector of genes in the identified DNB module

CI_all List of data.frames with CI scores for all candidate modules in each state

Gene_module List of gene modules detected in each state

Candidate Data.frame summarizing the best candidate module per state

Cor List of correlation matrices for each state

V List of gene variation values for each state

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

References

Chen L, Liu R, Liu ZP, Li M, Aihara K. (2012). Detecting early-warning signals for sudden deterioration of complex diseases by dynamical network biomarkers. Scientific Reports, 2:342. doi:10.1038/srep00342

See Also

tDNB for topological DNB, LcDNB for local DNB with PPI, MDNB for module-based DNB

Examples

```
# Create example data
set.seed(42)
n_genes <- 100
n_samples <- 15

expr <- matrix(
  rnorm(n_genes * n_samples, mean = 10, sd = 2),
  nrow = n_genes, ncol = n_samples
)
rownames(expr) <- paste0("Gene", seq_len(n_genes))
colnames(expr) <- paste0("Sample", seq_len(n_samples))

state <- data.frame(
  sample_id = colnames(expr),
  state = rep(c("A", "B", "C"), each = 5)
)


result <- cDNB(
  expr = expr,
  state = state,
  state.levels = c("A", "B", "C"),
  min.size = 5,
  max.size = 50
)
result$DNB.score
```

LcDNB *Local Conventional DNB Analysis*

Description

Performs local conventional dynamic network biomarker (LcDNB) analysis using protein-protein interaction (PPI) networks.

Usage

```
LcDNB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  variation.method = "sd",
  min.first.neighbor.size = 3,
  min.second.neighbor.size = 1,
  ppi = ppi_h,
  min.combined.score = 900,
  percent = TRUE,
  top.n = 30,
  top.p = 0.05,
  AddModuleSize = FALSE
)
```

Arguments

`expr`	A numeric matrix with genes in rows and samples in columns.
`state`	A data.frame with sample IDs and state labels (2 columns).
`state.levels`	Character vector specifying the order of states.
`cor.method`	Correlation method: "pearson", "spearman", or "kendall".
`p.adjust.method`	P-value adjustment method. Default: "BH".
`variation.method`	Method for variation: "sd" or "cv". Default: "sd".
`min.first.neighbor.size`	Minimum first-order neighbors. Default: 3.
`min.second.neighbor.size`	Minimum second-order neighbors. Default: 1.
`ppi`	PPI network data.frame with G1, G2, combined_score columns.
`min.combined.score`	Minimum STRING score. Default: 900.
`percent`	Use percentage (TRUE) or absolute number (FALSE).

top.n	Number of top genes when percent=FALSE. Default: 30.
top.p	Proportion when percent=TRUE. Default: 0.05.
AddModuleSize	Weight by module size. Default: FALSE.

Value

A list containing DNB.score, DNB.genes, CI_all, Gene_module, Candidate, Cor, V, PPI.used, first.order.genes, second.order.genes.

Author(s)

Zaoqu Liu

See Also

cDNB, LDNB, ppi_h

Examples

```
# See vignette for detailed examples
```

LDNB *Landscape DNB Analysis*

Description

Performs landscape dynamic network biomarker (LDNB) analysis for detecting critical transitions. This method uses sample-specific perturbation networks (SSPN) to identify tipping points in biological state transitions.

Usage

```
LDNB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 990,
  min.first.neighbor.size = 10,
  min.second.neighbor.size = 1,
  use.PCC.P.type = "FDR",
  use.PCC.P.cutoff = 0.05,
  percent = FALSE,
```

```
  top.n = 30,
  top.p = 0.05,
  nCores = max(1, parallel::detectCores() - 2)
)
```

Arguments

`expr`	A numeric matrix or data.frame with genes in rows and samples in columns. Row names should be gene symbols.
`state`	A data.frame with exactly two columns: sample identifiers and state labels. Must include a `"ref"` state for reference samples.
`state.levels`	A character vector specifying the order of states. The first level should be `"ref"` (reference state).
`cor.method`	Character string specifying correlation method. One of `"pearson"` (default), `"spearman"`, or `"kendall"`.
`p.adjust.method`	Character string specifying p-value adjustment method. Default: `"BH"`.
`ppi`	A data.frame containing protein-protein interactions with columns `G1`, `G2`, and `combined_score`.
`min.combined.score`	Numeric. Minimum STRING combined score. Default: 990.
`min.first.neighbor.size`	Integer. Minimum first-order neighbors. Default: 10.
`min.second.neighbor.size`	Integer. Minimum second-order neighbors. Default: 1.
`use.PCC.P.type`	Character. Type of p-value for filtering: `"FDR"` (default) or `"NP"` (nominal p-value).
`use.PCC.P.cutoff`	Numeric. P-value cutoff. Default: 0.05.
`percent`	Logical. Use percentage (`top.p`) or absolute number (`top.n`). Default: `FALSE`.
`top.n`	Integer. Number of top genes when `percent = FALSE`. Default: 30.
`top.p`	Numeric. Proportion when `percent = TRUE`. Default: 0.05.
`nCores`	Integer. Number of CPU cores for parallel computation.

Details

LDNB analysis requires a reference state (labeled as `"ref"` in the state column) to construct background networks. The algorithm:

1. Constructs sample-specific perturbation networks (SSPN)
2. Calculates local landscape indices for each gene
3. Aggregates to global indices per sample and state
4. Identifies critical state and DNB genes

Value

A list containing:

state.GI Data.frame with global indices per state

DNB.genes Character vector of identified DNB genes

Gene.LI Data.frame of genes ranked by landscape index

case.GI Data.frame with global index per sample

case.LI.list List of local indices per sample

SSPN Sample-specific perturbation network results

Author(s)

Zaoqu Liu <liuzaoqu@163.com>

References

Liu R, et al. (2019). Single-sample landscape entropy reveals the imminent phase transition during disease progression. National Science Review, 7(7):775-785. doi:10.1093/nsr/nwy162

See Also

SSPN1, LcDNB, SLE

Examples

```
# LDNB requires a reference state
# See vignette for detailed examples
```

MDNB *Module-based Dynamic Network Biomarker (MDNB) Analysis*

Description

Performing module-based dynamic network biomarker analysis using PPI network

Usage

```
MDNB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  ppi = ppi_h,
  min.combined.score = 900,
```

```
  PCC.min = 0.02,
  PCC.module = 0.02,
  numeber.module.QI = 10
)
```

Arguments

`expr`	A expression dataframe with gene rows and sample columns.
`state`	A dataframe with two columns: sample names and group information.
`state.levels`	A vector for state sequence (e.g., cell groups, time points, treatment conditions).
`cor.method`	Specifies the method for correlation analysis.
`ppi`	Protein-protein interaction network; background network.
`min.combined.score`	Minimum combined score for determining protein-protein interaction.
`PCC.min`	Remove genes if their highest correlation with any other gene is less than this value.
`PCC.module`	A gene must maintain at least this minimum correlation with the seed gene in every group to be included in the module.
`numeber.module.QI`	Number of gene modules selected for QI calculation.

Value

A list containing:

- DNB.score: The DNB score values (QI values) calculated for different groups.
- DNB.genes: Genes from the module with highest CI in the critical state.
- CI_all: Module contribution index (CI) details for each state.
- Gene_module: Generated co-expression gene modules.
- QIplot: Line chart showing QI changes across states.
- metadata: Additional information about the analysis.

Author(s)

Zaoqu Liu, Chuhan Zhang; Email: liuzaoqu@163.com

References

Li L, Xu Y, Yan L, et al. Dynamic network biomarker factors orchestrate cell-fate determination at tipping points during hESC differentiation. Innovation (Camb). 2022 Dec 20;4(1):100364. doi: 10.1016/j.xinn.2022.100364

ppi_h *Human Protein-Protein Interaction Network*

Description

Protein-protein interaction network for human (Homo sapiens) from STRING database v12.0. This dataset contains interactions with confidence scores, suitable for network-based DNB analyses including LcDNB, MDNB, LDNB, TSNMB, and TSLE.

Usage

```
ppi_h
```

Format

A data frame with protein-protein interactions:

G1 Gene 1 symbol (character). First interacting gene.

G2 Gene 2 symbol (character). Second interacting gene.

combined_score Interaction confidence score (numeric, 0-999). Higher scores indicate stronger evidence for interaction. Typical cutoffs: 400 (medium), 700 (high), 900 (highest).

Details

Data Source: STRING database v12.0 (https://string-db.org/)

Species: Homo sapiens (NCBI Taxonomy ID: 9606)

Recommended Score Cutoffs:

- 400-600: Medium confidence (broad coverage)
- 700-800: High confidence (balanced)
- 900+: Highest confidence (most reliable)

Usage in DNB Analysis: Use this PPI network for human single-cell or bulk RNA-seq data with PPI-based DNB methods: LcDNB, MDNB, LDNB, TSNMB, TSLE.

Source

STRING database v12.0 https://string-db.org/ https://stringdb-downloads.org/

References

Szklarczyk D, et al. The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest. Nucleic Acids Res. 2023;51(D1):D638-D646.

See Also

ppi_m for mouse PPI network

Examples

```
# Load human PPI
data("ppi_h")

# Explore the network
dim(ppi_h)
head(ppi_h)

# Check gene coverage
all_genes <- unique(c(ppi_h$G1, ppi_h$G2))
length(all_genes)

# Filter by confidence
high_conf <- ppi_h[ppi_h$combined_score >= 700, ]
nrow(high_conf)
```

---

ppi_m *Mouse Protein-Protein Interaction Network*

Description

Protein-protein interaction network for mouse (Mus musculus) from STRING database v12.0. This dataset contains interactions with confidence scores, suitable for network-based DNB analyses including LcDNB, MDNB, LDNB, TSNMB, and TSLE.

Usage

```
ppi_m
```

Format

A data frame with 12,684,354 protein-protein interactions:

G1 Gene 1 symbol (character). First interacting gene.

G2 Gene 2 symbol (character). Second interacting gene.

combined_score Interaction confidence score (numeric, 0-999). Higher scores indicate stronger evidence for interaction. Typical cutoffs: 400 (medium), 700 (high), 900 (highest).

Details

Data Source: STRING database v12.0 (https://string-db.org/)

Species: Mus musculus (NCBI Taxonomy ID: 10090)

Statistics:

- Total interactions: 12,684,354
- Unique genes: 21,645

- Score range: 150-999

Recommended Score Cutoffs:

- 400-600: Medium confidence (broad coverage)
- 700-800: High confidence (balanced)
- 900+: Highest confidence (most reliable)

Usage in DNB Analysis: Use this PPI network for mouse single-cell or bulk RNA-seq data with PPI-based DNB methods: LcDNB, MDNB, LDNB, TSNMB, TSLE.

Source

STRING database v12.0 https://string-db.org/ https://stringdb-downloads.org/

References

Szklarczyk D, et al. The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest. Nucleic Acids Res. 2023;51(D1):D638-D646.

See Also

ppi_h for human PPI network

Examples

```
# Load mouse PPI
data("ppi_m")

# Explore the network
dim(ppi_m)
head(ppi_m)

# Check gene coverage
all_genes <- unique(c(ppi_m$G1, ppi_m$G2))
length(all_genes) # 21,645 genes

# Filter by confidence
high_conf <- ppi_m[ppi_m$combined_score >= 700, ]
nrow(high_conf)

## Not run:
# Use in DNB analysis
result <- MDNB(
  expr = mouse_expr,
  state = sample_groups,
  state.levels = c("Control", "Treatment"),
  ppi = ppi_m,
  min.combined.score = 700
)
```

```
## End(Not run)
```

SLE *Single-sample landscape entropy analysis*

Description

Performing single-sample landscape entropy analysis.

Usage

```
SLE(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 900,
  min.first.neighbor.size = 1,
  percent = TRUE,
  top.n = 30,
  top.p = 0.05,
  nCores = parallel::detectCores() - 10
)
```

Arguments

`expr`	A expression dataframe with gene rows and sample columns.
`state`	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
`state.levels`	A vector for state sequence.
`cor.method`	specifies the method for correlation analysis.
`p.adjust.method`	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
`ppi`	Protein-protein interaction network; background network.
`min.combined.score`	Minimum combined score for determining protein-protein interaction.
`min.first.neighbor.size`	Minimum size of first order genes of a specific center gene.
`percent`	Whether to use Percent to determine the number of DNB genes.
`top.n`	Only percent = FALSE takes effect. Center genes with top (number) DNB score were defined as DNB genes.

top.p	Only percent = TRUE takes effect. Center genes with top (percent) DNB score were defined as DNB genes.
nCores	The number of cores will be used.

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

---

sNMB *Single-sample network module biomarker analysis*

Description

Performing single-sample network module biomarker analysis.

Usage

```
sNMB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 900,
  min.first.neighbor.size = 3,
  percent = TRUE,
  top.n = 30,
  top.p = 0.05,
  nCores = parallel::detectCores() - 10
)
```

Arguments

expr	A expression dataframe with gene rows and sample columns.
state	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
state.levels	A vector for state sequence.
cor.method	specifies the method for correlation analysis.
p.adjust.method	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
ppi	Protein-protein interaction network; background network.
min.combined.score	Minimum combined score for determining protein-protein interaction.

min.first.neighbor.size
: Minimum size of first order genes of a specific center gene.

percent
: Whether to use Percent to determine the number of DNB genes.

top.n
: Only percent = FALSE takes effect. Center genes with top (number) DNB score were defined as DNB genes.

top.p
: Only percent = TRUE takes effect. Center genes with top (percent) DNB score were defined as DNB genes.

nCores
: The number of cores will be used.

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

SSPN1 *Sample-specific perturbation network based on PPI network*

Description

Performing sample-specific perturbation network analysis based on PPI network.

Usage

```
SSPN1(
  expr,
  ref.samples,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 900,
  nCores = parallel::detectCores() - 10
)
```

Arguments

expr
: A expression dataframe with gene rows and sample columns.

ref.samples
: Samples for constructing the background reference network; Column ID or names.

cor.method
: specifies the method for correlation analysis.

p.adjust.method
: correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")

ppi
: Protein-protein interaction network; background network.

min.combined.score
: Minimum combined score for determining protein-protein interaction.

nCores
: The number of cores will be used.

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

SSPN2 *Sample-specific perturbation network based on customized network*

Description

Performing sample-specific perturbation network analysis based on customized network.

Usage

```
SSPN2(
  expr,
  ref.samples,
  net,
  cor.method = "pearson",
  p.adjust.method = "BH",
  nCores = parallel::detectCores() - 10
)
```

Arguments

expr	A expression dataframe with gene rows and sample columns.
ref.samples	Samples for constructing the background reference network; Column ID or names.
net	A customized network with two columns.
cor.method	specifies the method for correlation analysis.
p.adjust.method	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
nCores	The number of cores will be used.

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

tDNB *Topological DNB analysis*

Description

Performing topological dynamic network biomarker analysis using scale-free network topology. This is a novel method developed by Liu Z. that leverages topological overlap matrix (TOM) for more robust DNB detection.

Usage

```
tDNB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  variation.method = "sd",
  min.size = 10,
  max.size = 2000,
  AddModuleSize = FALSE,
  power.vec = c(seq_len(10), seq(from = 12, to = 20, by = 2)),
  network.type = "signed",
  RsquaredCut = 0.85
)
```

Arguments

expr	A expression dataframe with gene rows and sample columns.
state	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
state.levels	A vector for state sequence.
cor.method	specifies the method for correlation analysis.
p.adjust.method	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
variation.method	specifies the method for calculating gene variation. sd or cv.
min.size	Minimum gene number of gene modules.
max.size	Maximum gene number of gene modules.
AddModuleSize	Whether to consider gene module size when calculating DNB score.
power.vec	a vector of soft thresholding powers for which the scale free topology fit indices are to be calculated.
network.type	network type. Allowed values are (unique abbreviations of) "unsigned" or "signed".
RsquaredCut	desired minimum scale free topology fitting index R^2.

Value

A list containing:

DNB.score A data.frame with composite index (CI) values for each state, including V_in (mean variation), R_in (mean correlation within DNB), and R_out (mean correlation with non-DNB genes)

DNB.genes Character vector of genes in the identified DNB module

CI_all List of data.frames with CI scores for all candidate modules in each state

Gene_module List of gene modules detected in each state

Candidate Data.frame summarizing the best candidate module per state

RawCor List of correlation matrices for each state

Tom List of topological overlap matrices for each state

V List of gene variation values for each state

SFNet List of scale-free network fitting results

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

Examples

```
# Create example data
set.seed(42)
n_genes <- 100
n_samples <- 15

expr <- matrix(
  rnorm(n_genes * n_samples, mean = 10, sd = 2),
  nrow = n_genes, ncol = n_samples
)
rownames(expr) <- paste0("Gene", seq_len(n_genes))
colnames(expr) <- paste0("Sample", seq_len(n_samples))

state <- data.frame(
  sample_id = colnames(expr),
  state = rep(c("A", "B", "C"), each = 5)
)


result <- tDNB(
  expr = expr,
  state = state,
  state.levels = c("A", "B", "C"),
  min.size = 5,
  max.size = 50
)
result$DNB.score
```

TSLE *Time-series landscape entropy analysis*

Description

Performing time-series landscape entropy analysis.

Usage

```
TSLE(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 900,
  min.first.neighbor.size = 3,
  percent = TRUE,
  top.n = 30,
  top.p = 0.05
)
```

Arguments

expr	A expression dataframe with gene rows and sample columns.
state	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
state.levels	A vector for state sequence.
cor.method	specifies the method for correlation analysis.
p.adjust.method	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
ppi	Protein-protein interaction network; background network.
min.combined.score	Minimum combined score for determining protein-protein interaction.
min.first.neighbor.size	Minimum size of first order genes of a specific center gene.
percent	Whether to use Percent to determine the number of DNB genes.
top.n	Only percent = FALSE takes effect. Center genes with top (number) DNB score were defined as DNB genes.
top.p	Only percent = TRUE takes effect. Center genes with top (percent) DNB score were defined as DNB genes.

Author(s)

Zaoqu Liu; E-mail: liuzaoqu@163.com

TSNMB *Time-series network module biomarker analysis*

Description

Performing time-series network module biomarker analysis.

Usage

```
TSNMB(
  expr,
  state,
  state.levels,
  cor.method = "pearson",
  p.adjust.method = "BH",
  ppi = ppi_h,
  min.combined.score = 900,
  min.first.neighbor.size = 3,
  percent = TRUE,
  top.n = 30,
  top.p = 0.05
)
```

Arguments

expr	A expression dataframe with gene rows and sample columns.
state	A time-series dataframe with two columns, the first is the sample names and the second is the group or time point information.
state.levels	A vector for state sequence.
cor.method	specifies the method for correlation analysis.
p.adjust.method	correction method, a character string. Can be abbreviated. c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")
ppi	Protein-protein interaction network; background network.
min.combined.score	Minimum combined score for determining protein-protein interaction.
min.first.neighbor.size	Minimum size of first order genes of a specific center gene.
percent	Whether to use Percent to determine the number of DNB genes.
top.n	Only percent = FALSE takes effect. Center genes with top (number) DNB score were defined as DNB genes.
top.p	Only percent = TRUE takes effect. Center genes with top (percent) DNB score were defined as DNB genes.

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