Package 'Mirsynergy'

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Type Package

Title Mirsynergy

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Description Detect synergistic miRNA regulatory modules by overlapping neighbourhood expansion.

Depends R (>= 3.0.2), igraph, ggplot2

Imports graphics, grDevices, gridExtra, Matrix, parallel, RColorBrewer, reshape, scales, utils

Suggests glmnet, RUnit, BiocGenerics, knitr

License GPL-2

URL http://www.cs.utoronto.ca/~yueli/Mirsynergy.html

biocViews Clustering

Lazyload yes

VignetteBuilder knitr

git_url https://git.bioconductor.org/packages/Mirsynergy

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R topics documented:

`Mirsynergy-package` *Mirsynergy: detect synergistic miRNA regulatory modules by overlapping neighbourhood expansion.*

Description

Mirsynergy is a deterministic overlapping clustering algorithm adapted from a recently developed framework. Mirsynergy operates in two stages that first forms MRM based on co-occurring miRNAs and then expand the MRM by greedily including (excluding) mRNA into (from) the MRM to maximize the synergy score, which is a function of miRNA-mRNA and gene-gene interactions.

Details

Package:	Mirsynergy
Type:	Package
Version:	0.99.2
Date:	2014-02-06
License:	GPL-2

The main function `mirsynergy` takes as inputs the mRNA and miRNA interaction matrix and gene-gene interaction matrix provided by the user or generated from existing techniques described in the manuscript (in preparation). The function then outputs a list with each item as a miRNA regulatory module (MRM) containing miRNA and mRNA ID and and other results for diagnostic purpose.

Author(s)

Yue Li Maintainer: Yue Li <yueli@cs.toronto.edu>

References

Li, Y. et al. Mirsynergy: detect synergistic miRNA regulatory modules by overlapping neighbourhood expansion. (in preparation).

Nepusz, T., Yu, H., & Paccanaro, A. (2012). Detecting overlapping protein complexes in protein-protein interaction networks. Nature Methods, 9(5), 471-472. doi:10.1038/nmeth.1938

See Also

`mirsynergy`

`mirsynergy` *Detect synergistic miRNA regulatory modules by overlapping neighbourhood expansion*

Description

Detect synergistic miRNA regulatory modules by overlapping neighbourhood expansion using a deterministic overlapping clustering algorithm adapted from a recently developed framework. Mirsynergy operates in two stages that first forms MRM based on co-occurring miRNAs and then expand the MRM by greedily including (excluding) mRNA into (from) the MRM to maximize the synergy score, which is a function of miRNA-mRNA and gene-gene interactions.

Usage

```
mirsynergy(W, H, alpha = 2, merge.tol = 0.8,
  density1.tol = 1e-2, density2.tol=5e-3, verbose = FALSE)
```

Arguments

W	An N by M edge weight matrix containing interaction strength between N mRNA and M miRNA.
H	An N by N edge weight matrix containing the binary interaction among the N mRNA (genes).
alpha	Penalty for including a node into the growing module (advanced option). See manuscript or Nepusz et al. (2012) for more details.
merge.tol	Threshold with range [0,1] to merge modules based on the percentage of nodes shared between the two modules.
density1.tol	Threshold with range [0,1] to filter modules by the density function at stage 1 clustering.
density2.tol	Threshold with range [0,1] to filter modules by the density function 2 at stage 2 clustering.
verbose	Binary indicator to show running info.

Details

The weight matrix W can be obtained by various approaches such as Pearson correlation or linear regression on mRNA and miNRA expression profiles across multiple samples. Matrix H can be obtained from public database such as TRANSFAC and BioGrid.

Value

A nested list containing each item as a miRNA regulatory module (MRM). Each item itself is a list containing the following information:

miRNA	miRNA included in the MRM
mRNA	mRNA included in the MRM
v.in	miRNA and mRNA
v.bound	miRNA and mRNA disregard or excluded from the MRM but still have nonzero connection with the internal nodes
card.m	Number of miRNA in the MRM
card.t	Number of mRNA targets in the MRM
card	Total number of miRNA and mRNA targets in the MRM
density	Density of the MRM

Author(s)

Yue Li

References

Nepusz, T., Yu, H., & Paccanaro, A. (2012). Detecting overlapping protein complexes in protein-protein interaction networks. Nature Methods, 9(5), 471-472. doi:10.1038/nmeth.1938

Examples

```
##---- Should be DIRECTLY executable !! ----
##-- ==>  Define data, use random,
##--or do  help(data=index)  for the standard data sets.
##
# simulate N mRNA and M miRNA and their interaction matrices
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

# run mirsynergy clustering
V <- mirsynergy(W, H, verbose=TRUE)

summary_modules(V)
```

`plot_modules` *Plot module assignments.*

Description

Plot as network graphical view of the output from `mirsynergy` `V`. NB: small network only.

Usage

```
plot_modules(V, W, H, legend.pos = "topright", ...)
```

Arguments

`V`	Outputs from `mirsynergy`
`W`	An N by M edge weight matrix containing interaction strength between N mRNA and M miRNA.
`H`	An N by N edge weight matrix containing the binary interaction among the N mRNA (genes).
`legend.pos`	Specify legend position
`...`	Other parameters passed to `plot`

Details

Each node will be coloured by the modules they belong to. If a node belongs to multiple modules, it will be coloured differently based on the exact combination of the module indexes. The legend displays the corresponding colours and module assignments.

Note

Only for small network. For large network please use `tabular_module` to create a pairwise table as input to Cytoscape.

Author(s)

Yue Li

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

plot_modules(V,W,H)
```

`plot_module_summary` *Plot module statistics*

Description

Plot module statistics using output from `mirsynergy`.

Usage

```
plot_module_summary(V)
```

Arguments

`V`	Outputs from `mirsynergy`

Author(s)

Yue Li

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

plot_module_summary(V)
```

print_modules2 *Print basic information of the formed modules*

Description

Print basic information of the formed modules.

Usage

```
print_modules2(V)
```

Arguments

V	Output from mirsynergy.

Author(s)

Yue Li

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

print_modules2(V)
```

summary_modules *Return summary information of the formed modules*

Description

Return summary information of the formed modules, which are the outputs from mirsynergy

Usage

```
summary_modules(V)
```

Arguments

V	Output from mirsynergy.

Value

moduleSummaryInfo	Summary information per module
miRNA.internal	miRNA count distribution across modules
mRNA.internal	mRNA count distribution across modules

Author(s)

Yue Li

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

summary_modules(V)
```

`tabular_module` *Generate tabulated module assignments and nodes for input to Cystoscape.*

Description

Generate tabulated module assignments and nodes for input to Cystoscape.

Usage

```
tabular_module(V, W, H, outdir)
```

Arguments

`V`	Output from `mirsynergy`.
`W`	An N by M edge weight matrix containing interaction strength between N mRNA and M miRNA.
`H`	An N by N edge weight matrix containing the binary interaction among the N mRNA (genes).
`outdir`	Path to save the nodes and edges files.

Value

`nodes`	data.frame containing edges in each indexed module. Each edge (row) contain the edge weights, the edge type (MMI or GGI), and which module they belong to.
`edges`	data.frame containing nodes in each indexed module. Each node (row) contain the node name, type (mRNA/miRNA), and which module they belong to.

Author(s)

Yue Li

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))

tabular_module(V,W,H)
```

tcga_brca_testdata *Breast cancer expression test data from TCGA*

Description

Test data of 2661 mRNA and 142 miRNA (i.e., 0.2 of the whole data) across 15 tumor samples from breast cancer (BRCA) patients. The data were downloaded from TCGA (The Cancer Genome Atlas). The full BRCA expression data contain expression measurements for 13306 and 710 distinct mRNAs and miRNAs across 331 samples.

Format

A list containing the follow items:

X,Z N-by-T and M-by-T Expression matrices for N mRNA and M miRNA measured across T samples

C,H N-by-M and N-by-N matrices for sequence-based miRNA-targets downloaded from TargetScan-Human 6.2 and gene-gene interactions from TRANSFAC and BioGrid invoving transcription factor binding sites (TFBS) and protein-protein interactions, respectively.

References

Cancer Genome Atlas Research Network (2008). Comprehensive genomic characterization defines human glioblastoma genes and core pathways. Nature, 455(7216), 1061-1068.

Friedman, R. C., Farh, K. K.-H., Burge, C. B., and Bartel, D. P. (2009). Most mammalian mRNAs are conserved targets of microRNAs. Genome Research, 19(1), 92-105.

Examples

```
load(system.file("extdata/tcga_brca_testdata.RData", package="Mirsynergy"))
```

toy_modules *Test data of 20 mRNA and 20 miRNA.*

Description

Test data of 20 mRNA and 20 miRNA generated from simulation.

Format

A list containing the follow items:

V Outputs from `mirsynergy`

W,H Inputs used to generate V

Examples

```
load(system.file("extdata/toy_modules.RData", package="Mirsynergy"))
```

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