

Package ‘GNET2’

October 17, 2020

Type Package

Title Constructing gene regulatory networks from expression data through functional module inference

Version 1.4.0

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Description Cluster genes to functional groups with E-M process. Iteratively perform TF assigning and Gene assigning, until the assignment of genes did not change, or max number of iterations is reached.

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Encoding UTF-8

LazyData true

LinkingTo Rcpp

Depends R (>= 3.3)

Imports

ggplot2,xgboost,Rcpp,reshape2,grid,DiagrammeR,methods,stats,matrixStats,graphics,SummarizedExperiment,dplyr,i
grDevices

RoxygenNote 7.0.2

Suggests knitr, rmarkdown

VignetteBuilder knitr

biocViews GeneExpression, Regression, Network, NetworkInference,
Software

URL <https://github.com/chrischen1/GNET2>

BugReports <https://github.com/chrischen1/GNET2/issues>

git_url <https://git.bioconductor.org/packages/GNET2>

git_branch RELEASE_3_11

git_last_commit 06ae06d

git_last_commit_date 2020-04-27

Date/Publication 2020-10-16

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build_module	<i>Fit a regression tree.</i>
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Description

Fit a regression tree based on Gaussian Likelihood score. Provided in case the best split is not applicable for R `dnorm()` function.

Usage

```
build_module(X, Y, max_depth, cor_cutoff, min_divide_size)
```

Arguments

X	A n by p matrix as input.
Y	A n by q matrix as response.
max_depth	Maximum depth of the tree.
cor_cutoff	Cutoff for within group Pearson correlation coefficient, if all data belong to a node have average correlation greater or equal to this, the node would not split anymore.
min_divide_size	Minimum number of data belong to a node allowed for further split of the node.

Value

A matrix for sample information for each partition level. First column is feature index used by the node and second is the value used to split, the rest of the columns are the split of sample: 0 means less or equal, 1 means greater and -1 means the sample does not belong to this node.

Examples

```
build_module(X = matrix(rnorm(5*10),5,10), Y = matrix(rnorm(5*10),5,10),
               max_depth=3,cor_cutoff=0.9,min_divide_size=3)
```

build_moduleR	<i>Build regression tree.</i>
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Description

Build regression tree based on Gaussian Likelihood score.

Usage

```
build_moduleR(X, Y, max_depth, cor_cutoff, min_divide_size)
```

Arguments

X	A n by p matrix as input.
Y	A n by q matrix as response.
max_depth	Maximum depth of the tree.
cor_cutoff	Cutoff for within group Pearson correlation coefficient, if all data belong to a node have average correlation greater or equal to this, the node would not split anymore.
min_divide_size	Minimum number of data belong to a node allowed for further split of the node.

Value

A matrix for sample information for each tree level. First column is feature index used by the node and second is the value used to split, the rest of the columns are the split of sample: 0 means less or equal, 1 means greater and -1 means the sample does not belong to this node.

Examples

```
build_moduleR(X = matrix(rnorm(5*10),5,10), Y = matrix(rnorm(5*10),5,10),
  max_depth=3,cor_cutoff=0.9,min_divide_size=3)
```

build_moduleR_heuristic	
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Build regression tree with splits are determined by K-means heuristically.

Description

Build regression tree based on Gaussian Likelihood score. The splitting of the tree is determined heuristically by k_means.

Usage

```

build_moduleR_heuristic(
  X,
  Y,
  max_depth,
  cor_cutoff,
  min_divide_size,
  split_table
)

```

Arguments

X	A n by p matrix as input.
Y	A n by q matrix as response.
max_depth	Maximum depth of the tree.
cor_cutoff	Cutoff for within group Pearson correlation coefficient, if all data belong to a node have average correlation greater or equal to this, the node would not split anymore.
min_divide_size	Minimum number of data belong to a node allowed for further split of the node.
split_table	split table generated by K-means with build_split_table()

Value

A matrix for sample information for each tree level. First column is feature index used by the node and second is the value used to split, the rest of the columns are the split of sample: 0 means less or equal, 1 means greater and -1 means the sample does not belong to this node.

Examples

```

X <- matrix(rnorm(5*10),5,10)
build_moduleR_heuristic(X = X, Y = matrix(rnorm(5*10),5,10),max_depth=3,cor_cutoff=0.9,
  min_divide_size=3,split_table = build_split_table(X))

```

build_split_table	<i>Build split table by K-means heuristicly.</i>
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Description

Build split table by K-means with 3 cluster centers for each column of X

Usage

```
build_split_table(X)
```

Arguments

X	A n by p matrix as input.
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Value

A n by p matrix with each column consists of 3 clusters: -1 for low, 0 for mid and 1 for high

Examples

```
split_table <- build_split_table(matrix(rnorm(5*10),5,10))
```

calc_likelihood_score *Calculate Gaussian Likelihood score.*

Description

Calculate Gaussian Likelihood score.

Usage

```
calc_likelihood_score(x, group_labels)
```

Arguments

x A n by p matrix.
group_labels A vector of length n, indicating the group of rows.

Value

The sum of log likelihood score of each group on each column.

Examples

```
calc_likelihood_score(x = matrix(rnorm(5*10),5,10), group_labels = c(rep(1,2),rep(2,3)))
```

extract_edges *Extract the network from the gnet result*

Description

Extract the network as edge list from the gnet result. For a module, each regulator and downstream gene will form a directed edge.

Usage

```
extract_edges(gnet_result)
```

Arguments

gnet_result Returned results from gnet().

Value

A three column edge list from the gnet result. The third column are the sum of scores of any groups with the regulator-target interaction.

Examples

```

set.seed(1)
init_group_num = 8
init_method = 'kmeans'
exp_data <- matrix(rnorm(50*10),50,10)
reg_names <- paste0('TF',1:5)
rownames(exp_data) <- c(reg_names,paste0('gene',1:(nrow(exp_data)-length(reg_names))))
colnames(exp_data) <- paste0('condition_',1:ncol(exp_data))
se <- SummarizedExperiment::SummarizedExperiment(assays=list(counts=exp_data))
gnet_result <- gnet(se,reg_names,init_method,init_group_num)
edge_list <- extract_edges(gnet_result)

```

`get_correlation_list` *Calculate correlation within each group.*

Description

Calculate Pearson correlation coefficient within each group.

Usage

```
get_correlation_list(x, group_labels)
```

Arguments

`x` A n by p matrix.
`group_labels` A vector of length n, indicating the group of rows.

Value

An array of Pearson correlation coefficient for each row, rows belong to the same group have same values.

Examples

```
get_correlation_list(x = matrix(rnorm(5*10),5,10), group_labels = c(rep(1,2),rep(2,3)))
```

`gnet`

Run GNET2

Description

Build regulation modules by iteratively perform regulator assigning and Gene assigning, until the assignment of genes did not change, or max number of iterations reached.

Usage

```
gnet(
  input,
  reg_names,
  init_method = "boosting",
  init_group_num = 4,
  max_depth = 3,
  cor_cutoff = 0.9,
  min_divide_size = 3,
  min_group_size = 2,
  max_iter = 5,
  heuristic = TRUE,
  max_group = 0,
  force_split = 0.5
)
```

Arguments

<code>input</code>	A SummarizedExperiment object, or a p by n matrix of expression data of p genes and n samples, for example log2 RPKM from RNA-Seq.
<code>reg_names</code>	A list of potential upstream regulators names, for example a list of known transcription factors.
<code>init_method</code>	Cluster initialization, can be "boosting" or "kmeans", default is using "boosting".
<code>init_group_num</code>	Initial number of function clusters used by the algorithm.
<code>max_depth</code>	<code>max_depth</code> Maximum depth of the tree.
<code>cor_cutoff</code>	Cutoff for within group Pearson correlation coefficient, if all data belong to a node have average correlation greater or equal to this, the node would not split anymore.
<code>min_divide_size</code>	Minimum number of data belong to a node allowed for further split of the node.
<code>min_group_size</code>	Minimum number of genes allowed in a group.
<code>max_iter</code>	Maximum number of iterations allowed if not converged.
<code>heuristic</code>	If the splits of the regression tree is determined by k-means heuristically.
<code>max_group</code>	Max number of group allowed for the first clustering step, default equals <code>init_group_num</code> and is set to 0.
<code>force_split</code>	Force split the largest gene group into smaller groups by kmeans. Default is 0.5(Split if it contains more than half target genes)

Value

A list of expression data of genes, expression data of regulators, within group score, table of tree structure and final assigned group of each gene.

Examples

```
set.seed(1)
init_group_num = 8
init_method = 'boosting'
exp_data <- matrix(rnorm(50*10),50,10)
reg_names <- paste0('TF',1:5)
```

```
rownames(exp_data) <- c(reg_names,paste0('gene',1:(nrow(exp_data)-length(reg_names))))
colnames(exp_data) <- paste0('condition_',1:ncol(exp_data))
se <- SummarizedExperiment::SummarizedExperiment(assays=list(counts=exp_data))
gnet_result <- gnet(se,reg_names,init_method,init_group_num)
```

kneepointDetection *Knee point detection.*

Description

Detect the knee point of the array.

Usage

```
kneepointDetection(vect)
```

Arguments

vect A list of sorted numbers.

Value

The index of the data point which is the knee.

Examples

```
kneepointDetection(sort(c(runif(10,1,3),c(runif(10,5,10))),TRUE))
```

plot_gene_group *Plot a module*

Description

Plot the regulators module and heatmap of the expression inferred downstream genes for each sample. It can be interpreted as two parts: the bars at the top shows how samples are splited by the regression tree and the heatmap at the bottom shows how downstream genes are regulated by each subgroup determined by the regulators.

Usage

```
plot_gene_group(gnet_result, group_idx, tree_layout = 1, max_gene_num = 100)
```

Arguments

gnet_result Results returned by gnet().

group_idx Index of the module.

tree_layout zoom ratio for the regulatory tree. Default is 1. Need to be increased for trees with >5 regulators.

max_gene_num Max size of gene to plot in the heatmap. Only genes with highest n variances will be kept.

Value

None

Examples

```
set.seed(1)
init_group_num = 5
init_method = 'boosting'
exp_data <- matrix(rnorm(50*10),50,10)
reg_names <- paste0('TF',1:5)
rownames(exp_data) <- c(reg_names,paste0('gene',1:(nrow(exp_data)-length(reg_names))))
colnames(exp_data) <- paste0('condition_',1:ncol(exp_data))
se <- SummarizedExperiment::SummarizedExperiment(assays=list(counts=exp_data))
gnet_result <- gnet(se,reg_names,init_method,init_group_num)
plot_gene_group(gnet_result,group_idx=1)
```

plot_group_correlation

Plot the correlation of each group

Description

Plot the correlation of each group and auto detected knee point. It can be used to determined which clustered are kept for further analysis.

Usage

```
plot_group_correlation(gnet_result)
```

Arguments

`gnet_result` Results returned by `gnet()`.

Value

A list of indices of the data point with correlation higher than the knee point.

Examples

```
set.seed(1)
gnet_result <- list('group_score'=c(runif(10,1,3),c(runif(10,5,3))))
group_keep <- plot_group_correlation(gnet_result)
```

plot_tree	<i>Plot the regression tree.</i>
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Description

Plot the regression tree given the index of a module.

Usage

```
plot_tree(gnet_result, group_idx)
```

Arguments

gnet_result	Results returned by gnet().
group_idx	Index of the module.

Value

None

Examples

```
set.seed(1)
init_group_num = 5
init_method = 'boosting'
exp_data <- matrix(rnorm(50*10),50,10)
reg_names <- paste0('TF',1:5)
rownames(exp_data) <- c(reg_names,paste0('gene',1:(nrow(exp_data)-length(reg_names))))
colnames(exp_data) <- paste0('condition_',1:ncol(exp_data))
se <- SummarizedExperiment::SummarizedExperiment(assays=list(counts=exp_data))
gnet_result <- gnet(se,reg_names,init_method,init_group_num)
plot_tree(gnet_result,group_idx=1)
```

save_gnet	<i>Save the GNET2 results</i>
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Description

Save the edge list, group index of each gene and plot the top groups

Usage

```
save_gnet(gnet_result, save_path = ".", num_module = 10, max_gene_num = 100)
```

Arguments

gnet_result	Results returned by gnet().
save_path	path to save files
num_module	The number of modules with highest score to plot.
max_gene_num	The max number of genes to show in the heatmap.

Value

None

Examples

```
set.seed(1)
init_group_num = 5
init_method = 'boosting'
exp_data <- matrix(rnorm(50*10),50,10)
reg_names <- paste0('TF',1:5)
rownames(exp_data) <- c(reg_names,paste0('gene',1:(nrow(exp_data)-length(reg_names))))
colnames(exp_data) <- paste0('condition_',1:ncol(exp_data))
se <- SummarizedExperiment::SummarizedExperiment(assays=list(counts=exp_data))
gnet_result <- gnet(se,reg_names,init_method,init_group_num)
save_gnet(gnet_result)
```

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