Package ‘GNET2’

March 11, 2024

Type Package
Title Constructing gene regulatory networks from expression data through functional module inference
Version 1.18.0
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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.
License Apache License 2.0
Encoding UTF-8
LazyData true
LinkingTo Rcpp
Depends R (>= 3.6)
Imports ggplot2, xgboost, Rcpp, reshape2, grid, DiagrammeR, methods, stats, matrixStats, graphics, SummarizedExperiment, dplyr, igraph, grDevices, utils
RoxygenNote 7.1.0
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_18
git_last_commit 49bc07b
git_last_commit_date 2023-10-24
Repository Bioconductor 3.18
Date/Publication 2024-03-11
**R topics documented:**

- `build_module` .................................................. 2
- `build_moduleR` .................................................. 3
- `build_moduleR_heuristic` ..................................... 4
- `build_split_table` ............................................. 5
- `calc_likelihood_score` ........................................ 5
- `extract_edges` .................................................. 6
- `get_correlation_list` .......................................... 6
- `gnet` .................................................................. 7
- `kneepointDetection` ............................................. 8
- `plot_gene_group` .................................................. 9
- `plot_group_correlation` ......................................... 10
- `plot_tree` .......................................................... 11
- `save_gnet` ......................................................... 11
- `similarity_score` ................................................. 12

**Index**

14

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**build_module**

*Fit a regression tree.*

**Description**

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

**Usage**

```r
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**

```r
built_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**  
*Build regression tree.*

**Description**

Build regression tree based on Gaussian Likelihood score.

**Usage**

```r
built_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**

```r
built_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

*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**

```r
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**

```r
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  

Build split table by K-means heuristically.

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.

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)))
**get_correlation_list**

Calculate correlation within each group.

**Usage**

```r
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.

**Description**

Calculate Pearson correlation coefficient within each group.
Value

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

Examples

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

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

```r
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,
  nthread = 4
)
```

Arguments

- **input**: 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.
- **reg_names**: A list of potential upstream regulators names, for example a list of known transcription factors.
- **init_method**: Cluster initialization, can be "boosting" or "kmeans", default is using "boosting".
- **init_group_num**: Initial number of function clusters used by the algorithm.
- **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.
kneepointDetection

minute_divide_size
Minimum number of data belong to a node allowed for further split of the node.

min_group_size
Minimum number of genes allowed in a group.

max_iter
Maxumum number of iterations allowed if not converged.

heuristic
If the splits of the regression tree is determined by k-means heuristically.

max_group
Max number of group allowed for the first clustering step, default equals init_group_num and is set to 0.

force_split
Force split the largest gene group into smaller groups by kmeans. Default is 0.5(Split if it contains more than half target genes)

nthread
Number of threads to run GBDT based clustering

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(vect)

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

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

---

### 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

```r
plot_gene_group(
  gnet_result, 
  group_idx, 
  tree_layout = 1, 
  max_gene_num = 100, 
  plot_leaf_labels = TRUE, 
  group_labels = NULL
)
```

### 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.
- `plot_leaf_labels`  If the plot includes a color bar of leaf labels at the bottom.
- `group_labels`  Labels of experiment conditions. Used for the color bar of experiment conditions. Default is `NULL`.

### Value

None
Examples

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

```r
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

```r
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

**Plot the regression tree.**

**Description**

Plot the regression tree given the index of a module.

**Usage**

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

**Arguments**

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

**Value**

None

**Examples**

```r
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

**Save the GNET2 results**

**Description**

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

**Usage**

```r
save_gnet(gnet_result, save_path = '.', num_module = 10, max_gene_num = 100)
```
## similarity_score

### 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

```r
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)
```

---

### Description

Compute the similarity between a predefined condition grouping and the sample cluster of each module, which is defined as the Adjusted Rand index between the two vectors, or the inverse of K-L divergence between the upper triangle matrix of the pairwise distance of predefined ranked condition grouping and the pairwise distance of sample cluster of each module.

### Usage

```r
similarity_score(gnet_result, group, ranked = FALSE)
```

### Arguments

- **gnet_result**: Returned results from `gnet()`. 
- **group**: predefined condition grouping. 
- **ranked**: the grouping information is categorical(treatment/control) or ordinal(dosage, time points)?

### Value

A list of similarity scores between a predefined condition grouping and the sample cluster of each module, and the p values for the similarity scores based on permutation.
similarity_score

Examples

```r
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)
s <- similarity_score(gnet_result,rep(1:5,each = 2))
```
Index

build_module, 2
build_moduleR, 3
build_moduleR_heuristic, 4
build_split_table, 5

calc_likelihood_score, 5
extract_edges, 6
get_correlation_list, 6
gnet, 7

kneepointDetection, 8
plot_gene_group, 9
plot_group_correlation, 10
plot_tree, 11

save_gnet, 11
similarity_score, 12