Package ‘GNET2’

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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

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 informatrion 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_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)

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

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)
built_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

```r
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

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

---

**calc_likelihood_score**  

Calculate Gaussian Likelihood score.

Description

Calculate Gaussian Likelihood score.

Usage

```r
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

```r
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 matrix of scores of for the regulator-target interaction.

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)
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**

```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

min_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
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))

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 split 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,  
plot_leaf_labels = TRUE,  
group_labels = NULL
)

Arguments

  gnet_result   
  group_idx   
  tree_layout   
  max_gene_num   
  plot_leaf_labels   
  group_labels   

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)
```

---

```r
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
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
Save the GNET2 results

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)
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)
```

similarity_score **Compute the similarity from a predefined condition group**

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.
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))
```
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