Package ‘Pigengene’

Type Package

Title Infers biological signatures from gene expression data

Version 1.28.0

Date 2016-03-31

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biocViews GeneExpression, RNASeq, NetworkInference, Network, GraphAndNetwork, BiomedicalInformatics, SystemsBiology, Transcriptomics, Classification, Clustering, DecisionTree, DimensionReduction, PrincipalComponent, Microarray, Normalization, ImmunoOncology

Depends R (>= 4.0.3), graph, BiocStyle (>= 2.28.0)

Description Pigengene package provides an efficient way to infer biological signatures from gene expression profiles. The signatures are independent from the underlying platform, e.g., the input can be microarray or RNA Seq data. It can even infer the signatures using data from one platform, and evaluate them on the other. Pigengene identifies the modules (clusters) of highly coexpressed genes using coexpression network analysis, summarizes the biological information of each module in an eigengene, learns a Bayesian network that models the probabilistic dependencies between modules, and builds a decision tree based on the expression of eigengenes.

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Imports bnlearn (>= 4.7), C50 (>= 0.1.2), MASS, matrixStats, partykit, Rgraphviz, WGCNA, GO.db, impute, preprocessCore, grDevices, graphics, stats, utils, parallel, pheatmap (>= 1.0.8), dplyr, gdata, clusterProfiler, ReactomePA, ggplot2, openxlsx, DBI, DOSE

Suggests org.Hs.eg.db (>= 3.7.0), org.Mm.eg.db (>= 3.7.0), biomaRt (>= 2.30.0), knitr, AnnotationDbi, energy

VignetteBuilder knitr
NeedsCompilation no

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

git_branch RELEASE_3_18

git_last_commit 0294afc

git_last_commit_date 2023-10-24

Repository Bioconductor 3.18

Date/Publication 2024-02-20

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**Pigengene-package**  
*Infers robust biological signatures from gene expression data*

---

**Description**

Pigengene identifies gene modules (clusters), computes an eigengene for each module, and uses these biological signatures as features for classification. The resulting biological signatures are very robust with respect to the profiling platform. For instance, if Pigengene computes a biological signature using a microarray dataset, it can infer the same signature in an RNA Seq dataset such that it is directly comparable across the two datasets.

**Details**

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The main function is `one.step.pigengene` which requires a gene expression profile and the corresponding conditions (types). Individual functions are provided to facilitate running the pipeline in a customized way. Also, the inferred biological signatures (computed eigengenes) are useful for other supervised or unsupervised analyses.

In most functions of this package, eigengenes are computed or used as robust biological signatures. Briefly, each eigengene is a weighted average of the expression of all genes in a module (cluster), where the weights are adjusted in a way that the explained variance is maximized.

**Author(s)**

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Maintainer: Habil Zare <zare@txstate.edu>

**References**


**See Also**

Pigengene-package, one.step.pigengene, compute.pigengene, WGCNA::blockwiseModules
Examples

data(aml)
data(mds)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
p1 <- one.step.pigengene(Data=d1, saveDir="pigengene", bnNum=10, verbose=1,
seed=1, Labels=Labels, toCompact=FALSE, doHeat=FALSE)
plot(p1$c5treeRes$c5Trees["34"])
## See pigengene for results.

aml

  AML gene expression profile

Description

Gene expression profile of 202 acute myeloid leukemia (AML) cases from Mills et al. study. The profile was compared with the profile of 164 myelodysplastic syndromes (MDS) cases and only the 1000 most differentially expressed genes are included.

Usage

data("aml")

Format

A numeric matrix

Details

The columns and rows are named according to the genes Entrez, and patient IDs, respectively. The original data was produced using Affymetrix Human Genome U133 Plus 2.0 Miccoarray. Mills et al. study is part of the MILE Study (Microarray Innovations In LEukemia) program, and aimed at prediction of AML transformation in MDS.

Value

It is a 202*1000 numeric matrix.

Source


References

apply.filter

See Also

Pigengene-package, one.step.pigengene, mds.pigengene

Examples

library(pheatmap)
data(aml)
pheatmap(aml[,1:20],show_rownames=FALSE)

---

Description

Takes as input gamma and epsilon values and a filter graph, which is represented by an adjacency matrix named filt. Applies the filter on the data in either of the two ways: a) with normalization of the filter by degrees in the graph, b) without normalization.

Usage

apply.filter(gamma, filt, Data, doNormalize=FALSE)

Arguments

gamma This value is in the [0,1] range and determines the weight of the filter data. Setting to 0 will result in not filtering at all.

filt It is a binary matrix computed by the make.filter function.

Data A matrix or data frame (or list of matrices or data frames) containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named. For example, for RNA-Seq data, log(RPKM+1) can be used.

doNormalize If TRUE, the filter will be normalized by the degree in the graph using the filt * D^(-1), where D is a diagonal matrix with degrees of filt on its diagonal.

Value

filtered A filtered matrix computed using the gamma*sData formula, where sData is the scaled Data and filtN is the normalized or unnormalized filter.

Author(s)

Habil Zare and Neda Emami.

See Also

make.filter, determine.modules
Examples

data(aml)
data(mds)
d1 <- rbind(aml, mds)[, 1:200]
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)

p0 <- one.step.pigengene(Data=d1, saveDir=".", verbose=1,
                        seed=1, Labels=Labels, naTolerance=0.5,
                        RsquaredCut=0.8, doNetOnly=TRUE)

###Making the filter
made <- make.filter(network=p0$Network, epsilon=0.7, outPath=".")

###Applying the filter
f1 <- apply.filter(gamma=0.5, filt=made$filt, Data=d1)

---

**balance**

### Balances the number of samples

Description

Oversamples data by repeating rows such that each condition has roughly the same number of samples.

Usage

balance(Data, Labels, amplification = 5, verbose = 0, naTolerance=0.05)

Arguments

- **Data**: A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
- **Labels**: A (preferably named) vector containing the Labels (condition types) for Data. Names must agree with rows of Data.
- **amplification**: An integer that controls the number of repeats for each condition. The number of all samples roughly will be multiplied by this factor after oversampling.
- **verbose**: The integer level of verbosity. 0 means silent and higher values produce more details of computation.
- **naTolerance**: Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See check.pigengene.input.
calculate.beta

Value

A list of:

- balanced: The matrix of oversampled data
- Reptimes: A vector of integers named by conditions reporting the number of repeats for each condition.
- origSampleInds: The indices of rows in balanced that correspond to the original samples before oversampling

Author(s)

Habil Zare

See Also

Pigengene-package, one.step.pigengene, wgcna.one.step, compute.pigengene

Examples

data(aml)
data(mds)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
b1 <- balance(Data=d1, Labels=Labels)
d2 <- b1$balanced

calculate.beta (estimates an appropriate power value)

Description

The WGCNA package assumes that in the coexpression network the genes are connected with a power-law distribution. Therefore, it need a soft-thresholding power for network construction, which is estimated by this auxiliary function.

Usage

calculate.beta(saveFile = NULL, RsquaredCut = 0.8, Data, doThreads=FALSE, verbose = 0)
Arguments

saveFile  The file to save the results in. Set to NULL to disable.
RsquaredCut A threshold in the range [0,1] used to estimate the power. A higher value can increase power. For technical use only. See pickSoftThreshold for more details.
Data A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
doThreads Boolean. Allows WGCNA to run a little faster using multi-threading but might not work on all systems.
verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.

Value

A list of:
sft The full output of pickSoftThreshold function
power The estimated power (beta) value
powers The numeric vector of all tried powers
RsquaredCut The value of input argument RsquaredCut

References


See Also

pickSoftThreshold, blockwiseModules, one.step.pigengene, wgcna.one.step

Examples

data(aml)
p1 <- calculate.beta(Data=aml[,1:200])

check.nas  Removes NAs from a data matrix

Description

Checks Data for NA values.

Usage

check.nas(Data, naTolerance=0.05, na.rm=TRUE)
check.pigengene.input

Arguments

Data: A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.

naTolerance: A number in the 0-1 range. If the frequency of NAs in a column of Data is more than this threshold, then that column will be removed.

na.rm: If TRUE, NAs in the Data will be replaces with the average of the column, however, if the frequency of NAs in the column is too high (i.e., more than naTolerance), the whole column will be removed.

Value

A list of:

cleaned: The cleaned data with no NA value. Rows are the same as Data, but some columns may be deleted.

tooNaGenes: A character vector of those genes (i.e., column names of Data) that had too many NAs, and therefore were removed.

replacedNaNum: The number of NA entries in the matrix that were replaced with the average of the corresponding column (gene).

Author(s)

Habil Zare

See Also

check.pigengene.input, Pigengene-package

Examples

data(aml)
dim(aml)
aml[1:410]<-NA
c1 <- check.nas(Data=aml)
dim(c1$cleaned)
c1$tooNaGenes
rm(aml)

check.pigengene.input  Quality check on the input

Description

Checks Data and Labels for NA values, row and column names, etc.
Usage

```
check.pigengene.input(Data, Labels, na.rm = FALSE, naTolerance = 0.05)
```

Arguments

- **Data**
  A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.

- **Labels**
  A (preferably named) vector containing the Labels (condition types) for Data. Names must agree with rows of Data.

- **na.rm**
  If TRUE, NAs in the Data will be replaced with the average of the column, however, if the frequency of NAs in the column is too high, the whole column will be removed.

- **naTolerance**
  Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See `check.pigengene.input`.

Value

A list of:

- **Data**
  The checked Data matrix, NA possibly removed and rows are ordered as names of Labels.

- **Labels**
  The checked vector of Labels

Author(s)

Habil Zare

See Also

- `check.nas`
- `one.step.pigengene`
- `Pigengene-package`

Examples

```
data(aml)
Labels <- c(rep("AML", nrow(aml)))
names(Labels) <- rownames(aml)
c1 <- check.pigengene.input(Data=aml, Labels=Labels, na.rm=TRUE)
Data <- c1$Data
Labels <- c1$Labels
```
combine.networks

Combines two or more networks

Description

Takes as input two or more adjacency matrices, and the corresponding contributions. Computes a combined network (weighted graph) in which the weight on an edge between two nodes is an average of the weights on the same edge in the input networks.

Usage

```r
combine.networks(nets, contributions, outPath, midfix="", powerVector=1:20, verbose=1, RsquaredCut=0.75, minModuleSize=5, doRemoveTOM=TRUE, datExpr, doReturNetworks=FALSE, doSave=FALSE, doIdentifyModule=TRUE)
```

Arguments

- **nets**: A list of adjacency matrices (networks), which can be generated using e.g., the `WGCNA::adjacency` function. Rows and columns must be named.
- **contributions**: A numeric vector with the same length as nets. In computing the average weight on each edge in the combined network, first the edge weights from individual networks are multiplied by their corresponding contributions, then the result will be divided by the sum of weights of all networks containing this edge.
- **outPath**: A string to the path where plots and results will be saved.
- **midfix**: An optional string used in the output file names.
- **powerVector**: A numeric vector of power values that are tried to find the best one. See `WGCNA::pickSoftThreshold` documentation.
- **verbose**: The integer level of verbosity. 0 means silent and higher values produce more details of computation.
- **RsquaredCut**: A threshold in the range [0,1] used to estimate the power. A higher value can increase power. For technical use only. See `pickSoftThreshold` for more details.
- **minModuleSize**: The value that controls the minimum number of genes per module. See `WGCNA::blockwiseModules`.
- **doRemoveTOM**: A boolean determining the big TOM file must remove or not.
- **datExpr**: The expression matrix that WGCNA::blockwiseModules uses for fine-tuning and removing genes from modules. This is not an ideal behavior by WGCNA.
- **doReturNetworks**: A boolean value to determine whether to return Network, which is relatively a big matrix (typically GBs). Set to FALSE not to waste memory.
- **doSave**: A boolean value to determine whether the whole output of this function (typically 1-2 GBs) should be saved as combinedNetwork. Set to FALSE not to waste disk space.
- **doIdentifyModule**: A boolean value to determine whether modules should be identified. Set it to FALSE if you just need the network, not the modules.
Value

A list with following components:

- `call`: The command that created the results
- `midfix`: The input argument
- `Network`: The adjacency matrix of the combined network
- `denominators`: A matrix, each cell of which is the sum of weights of all networks contributing to the edge corresponding to that cell
- `power`: The power (beta) value used for the combined network
- `fits`: The fit indices calculated for the combined network
- `net`: The output of `WGCNA::blockwiseModules` containing the module information in its `colors` field
- `modules`: The output of `WGCNA::blockwiseModules`
- `combinedNetworkFile`: The path to the saved file containing `combinedNetwork`

Note

If the networks have different node sets, the combined network will be computed on the union of nodes.

See Also

`WGCNA::blockwiseModules`, `WGCNA::TOMsimilarity`, and `WGCNA::pickSoftThreshold.fromSimilarity`

Examples

```r
data(aml)
data(mds)
nets <- list()
## Make the coexpression networks:
nets["aml"] <- abs(stats::cor(aml[,1:200]))
nets["mds"] <- abs(stats::cor(mds[,1:200]))
## Combine them:
combined <- combine.networks(nets=nets, contributions=c(nrow(aml), nrow(mds)),
                             outPath=".", datExpr=rbind(aml, mds)[,1:200])
print(table(combined$modules))
```

compact.tree

Reduces the number of genes in a decision tree

Description

In a greedy way, this function removes the genes with smaller weight one-by-one, while assessing the accuracy of the predictions of the resulting trees.
**Usage**

```r
compact.tree(c5Tree, pigengene, Data=pigengene$Data, Labels=pigengene$Labels,
              testData=NULL, testLabels=NULL, saveDir=".", verbose=0)
```

**Arguments**

- **c5Tree**: A decision tree of class C5\(0\) that uses module eigengenes, or NULL. If NULL, expression plots for all modules are created.
- **pigengene**: A object of `pigengene-class`, output of `compute.pigengene`
- **Data**: A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
- **Labels**: Labels (condition types) for the (training) expression data. It is a named vector of characters. `Data` will be subset according to these names.
- **testD**: The test expression data, for example, from an independent dataset. Optional.
- **testL**: Labels (condition types) for the (test) expression data. Optional.
- **saveDir**: Where to save the plots of the tree(s)
- **verbose**: Integer level of verbosity. 0 means silent and higher values produce more details of computation.

**Value**

A list with following elements is invisibly returned:

- **call**: The call that created the results
- **predTrain**: Prediction using projected data without compacting
- **predTrainCompact**: Prediction after compacting
- **genes**: A character vector of all genes in the full tree before compacting
- **genesCompacted**: A character vector of all genes in the compacted tree
- **trainErrors**: A matrix reporting errors on the train data. The rows are named according to the number of removed genes. Each column reports the number of misclassified samples in one condition (type) except the last column that reports the total.
- **testErrors**: A matrix reporting errors on the test data similar to `trainErrors`
- **queue**: A numeric vector named by all genes contributing to the full tree before compacting. The numeric values are weights increasingly ordered by absolute value.
- **pos**: The number of removed genes
- **txtFile**: Confusion matrices and other details on compacting are reported in this text file

**References**


**compute.pigengene**

Computes the eigengenes

## Description

This function takes as input the expression data and module assignments, and computes an eigengene for each module using PCA.

## Usage

```r
compute.pigengene(Data, Labels, modules, saveFile = "pigengene.RData", selectedModules = "All", amplification = 5, doPlot = TRUE, verbose = 0, dOrderByW = TRUE, naTolerance=0.05, doWgcna=FALSE)
```

## Arguments

- **Data**: A matrix or data frame containing the training expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
- **Labels**: A (preferably named) vector containing the Labels (condition types) for the training Data. Names must agree with rows of Data.
- **modules**: A numeric vector, named by genes, that reports the module (clustering) assignments.
- **saveFile**: The file to save the results. NULL will disable saving, and thus requires `doPlot` to be FALSE.
- **selectedModules**: A numeric vector determining which modules to use, or set to "All" (default) to include every module.

## Examples

```r
## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml,mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1, saveDir="trees", minPerLeaf=14:15, doHeat=FALSE,verbose=3, toCompact=FALSE)
c1 <- compact.tree(c5Tree=trees$c5Trees[["15"]], pigengene=pigengene, saveDir="compacted", verbose=1)
```
amplification  An integer that controls the number of repeats for each condition. The number of all samples roughly will be multiplied by this factor after oversampling. See balance.
doPlot  Boolean determining whether heatmaps of expression of eigengenes should be plotted and saved. Set it to FALSE for large data to avoid memory exhaustion.
verbose  The integer level of verbosity. 0 means silent and higher values produce more details of computation.
dOrderByW  If TRUE, the genes will be ordered in the csv file based on their absolute weight in the corresponding module.
naTolerance  Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See check.pigengene.input.
doWgcna  If FALSE, prcomp will be used to compute PCA. Otherwise, WGCNA::blockwiseModules will be used leading to consuming more memory with no advantages.

Details

Rows of Data are oversampled using balance so that each condition has roughly the same number of samples. moduleEigengenes computes an eigengene for each module using PCA.

Value

An object of pigengene-class.

Author(s)

Habil Zare and Amir Foroushani

References


See Also

Pigengene-package, one.step.pigengene, wgcna.one.step, make.decision.tree, moduleEigengenes

Examples

## Data:
data(aml)
data(mds)
data(eigengenes33)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
modules33 <- eigengenes33$modules[colnames(d1)]
## Computing:
```r
pigengene <- compute.pigengene(Data=d1, Labels=Labels, modules=modules33, 
    saveFile="pigengene.RData", doPlot=TRUE, verbose=3)
class(pigengene)
plot(pigengene, fontsize=12)
```

### dcor.matrix

** Computes distance correlation for given matrix 

**Description**

This function computes the distance correlation between every pair of columns of the input data matrix.

**Usage**

```r
dcor.matrix(Data)
```

**Arguments**

- `Data` A matrix containing the data

**Details**

Using for loops, all pairs of columns are passed to `link[energy]{dcor}` function from `link[energy]{energy-package}`.

**Value**

A numeric square matrix. The number of rows and columns is equal to the number of columns of `Data` and they are named accordingly.

**Note**

This function uses for loops, which are not efficient for an input matrix with too many columns.

**Author(s)**

Habil Zare

**References**

<URL: http://dx.doi.org/10.1214/009053607000000505>

<URL: http://dx.doi.org/10.1214/09-AOAS312>

determine.modules

Identifies modules of the network

Description

Takes as input a network (i.e., weighted graph) and identifies modules (i.e., clusters of similar genes) using WGCNA::blockwiseModules. It also produces a plot showing the number of genes in each module.

Usage

determine.modules(network, outPath, midfix="", powerVector=1:20, verbose=1, RsquaredCut=0.75, minModuleSize=5, doRemoveTOM=FALSE, datExpr, doSave=FALSE)

Arguments

network An adjacency matrix of the network that is built using combine.networks.
outPath A string to the path where plots and results will be saved.
midfix An optional string used in the output file names.
powerVector A numeric vector of integer values that are tried to find the best power. See WGCNA::pickSoftThreshold.
verbose The integer level of verbosity, where 0 means silent and higher values produce more details.
RsquaredCut A threshold in the range [0,1] used to estimate the power. A higher value can increase power. For technical use only. See pickSoftThreshold for more details.

See Also

link[energy]{dcor}

Examples

## Data:
data(aml)
dcor1 <- dcor.matrix(Data=aml[,1:5])
dcor1

## Comparison with Pearson:
cor1 <- abs(stats::cor(aml[,1:5]))
## With 202 samples, distance and Pearson correlations do not differ much:
dcor1-corr1
dcor2 <- dcor.matrix(Data=aml[1:20,1:5])
cor2 <- abs(stats::cor(aml[1:20,1:5]))
## Distance correlation is more robust if fewer samples are available:
dcor2-cor2
plot(dcor2-cor1,cor1-cor2,xlim=c(-0.5,0.5),ylim=c(-0.5,0.5))
determine.modules

minModuleSize  The value that controls the minimum number of genes per module. See \texttt{WGCNA::blockwiseModules}.

doRemoveTOM  A boolean determining whether the big TOM file must remove or not.

datExpr  The expression matrix that \texttt{WGCNA::blockwiseModules} uses for fine-tuning and removing genes from modules. This is not an ideal behavior by WGCNA.

doSave  A boolean value to determine whether the whole output of this function (typically 1-2 GBs) should be saved as \texttt{combinedNetwork}. Set to FALSE not to waste disk space.

Value

A list with the following components:

- call  The call that created the results.
- midfix  The midfix input.
- power  The integer value of the estimated power computed by \texttt{pickSoftThreshold.fromSimilarity}.
- fits  The \texttt{fitIndices} output from \texttt{pickSoftThreshold.fromSimilarity}.
- modules  A vector that representing the identified modules. Its length is equal to the number of nodes in the network, named by node names (i.e., row names of \texttt{network}), and values are the corresponding module numbers.
- net  The full output of the \texttt{blockwiseModules} function.

Author(s)

Neda Emami and Habil Zare.

See Also

\texttt{apply.filter, combine.networks, make.filter}

Examples

data(aml)

##Making the coexpression network
network <- abs(stats::cor(aml[,1:200]))

##Identifying modules
identifiedMod <- determine.modules(network=network, outPath=".", datExpr=aml[,1:200])
print(table(identifiedMod$modules))
**draw.bn**

**Description**

Draws the BN using appropriate colors and font size.

**Usage**

```r
draw.bn(BN, plotFile = NULL, inputType = "ENTREZIDat", edgeColor = "blue", DiseaseCol = "darkgreen", DiseaseFill = "red", DiseaseChildFill = "pink", nodeCol = "darkgreen", nodeFill = "yellow", moduleNamesFile = NULL, mainText = NULL, nodeFontSize = 14 * 1.1, verbose = 0)
```

**Arguments**

- **BN** An object of `bn-class`
- **plotFile** If not NULL, the plot will be saved here.
- **inputType** The type of gene IDs in `BN`
- **edgeColor** The color of edges
- **DiseaseCol** The color of the border of the Disease node
- **DiseaseFill** The color of the area inside the Disease node
- **DiseaseChildFill** The color of the area inside the children of the Disease node
- **nodeCol** The color of the border of the usual nodes excluding Disease and its children
- **nodeFill** The color of the area inside the usual nodes
- **moduleNamesFile** An optional csv file including the information to rename the nodes name. See `coderename.node`.
- **mainText** The main text shown at the top of the plot
- **nodeFontSize** Adjusts the size of nodes
- **verbose** The integer level of verbosity. 0 means silent and higher values produce more details of computation.

**Value**

A list with following components:

- **call** The call that created the results
- **BN** An echo of input BN argument
- **renamedBN** An object of `bn-class` when `moduleNamesFile` is provided
- **gr** The full output of `graphviz.plot` function
**Author(s)**

Habil Zare

**See Also**

bnlearn-package, Pigengene-package, learn.bn, graph-class

**Examples**

```r
## See lear.bn function.
```

**Description**

This list contains partial eigengenes computed from AML and MDS gene expression profiles provided by Mills et al. These data are included to illustrate how to use Pigengene-package and also to facilitate reproducing the results presented in the corresponding paper.

**Usage**

```r
data(eigengenes33)
```

**Format**

A list

**Details**

The top 9166 differentially expressed genes were identified and their expressions in AML were used for identifying 33 modules. The first column, ME0, corresponds to module 0 (outliers) and is usually ignored. The eigengene for each module was obtained using compute.pigengene function. Oversampling was performed with amplification=5 to adjust for unbalanced sample-size.

**Value**

It is a list of 3 objects:

- `aml` A 202 by 34 matrix. Each column reports the values of a module eigengene for AML cases.
- `mds` A 164 by 34 matrix for MDS cases with columns similar to `aml`.
- `modules` A numeric vector of length 9166 labeling members of each module. Named by Entrez ID.

**Source**

gene.mapping

References


See Also

Pigengene-package, compute.pigengene.aml, mds, learn.bn

Examples

library(pheatmap)
data(eigengenes33)
pheatmap(eigengenes33$aml,show_rownames=FALSE)

## See Pigengene::learn.bn() documentation for more examples.

gene.mapping

Maps gene IDs

Description

Takse as input gene IDs in a convention, say REFSEQ, and converts them to another convention.

Usage

gene.mapping(ids, inputType = "REFSEQ", outputType = "SYMBOL",
leaveNA = FALSE, inputDb = "Human", outputDb = inputDb,
verbose = 0)

Arguments

ids A character vector of input gene IDs
inputType The type of input IDs.
outputType The type of output IDs. If it is a character vector, mapping will be done for each element.
leaveNA If TRUE, the IDs that were not matched are left with NAs in the second column of the output, otherwise (i.e., default) the input IDs are returned.
inputDb The input data base. Use org.Hs.eg.db for human and org.Mm.eg.db for mouse. The default "Human" character uses the former.
outputDb The output data base. If it is a list, mapping will be done for each element.
verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.

Details

It can map homologous genes between species e.g. from mouse to human. If more than 1 ID found for an input gene, only one of them is returned.
get.enriched.pw

Value

A matrix of characters with 3 columns: input, output1, and output2. The last one is guaranteed not to be NA if leaveNA=FALSE.

Author(s)

Amir Foroushani, Habil Zare, and Rupesh Agrahari

References

Pages H, Carlson M, Falcon S and Li N. AnnotationDbi: Annotation Database Interface. R package version 1.32.3.

See Also

AnnotationDb-class, org.Hs.eg.db org.Mm.eg.db

Examples

```r
library(org.Hs.eg.db)
g1 <- gene.mapping(ids="NM_001159995")
print(g1)

## Mapping to multiple convention
library(org.Mm.eg.db)
g2 <- gene.mapping(ids=c("NM_170730", "NM_001013580"),
                   inputType="REFSEQ", inputDb=org.Mm.eg.db,
                   outputType=c("SYMBOL","ENTREZID"),
                   outputDb=list(org.Hs.eg.db,org.Mm.eg.db), verbose=1)
print(g2)
```
Arguments

genes A character vector or a named list of genes for which pathway over representation analysis to be done.
idType A string describing the type of input gene ID e.g., "ENTREZID", "REFSEQ", "SYMBOL".
pathwayDb A character vector determining which enrichment database to be used e.g., "GO", "KEGG", "REACTOME", or "NCG".
ont GO ontology terms to be analysed e.g., "BP", "MF" or "CC". Default is all three.
Org A character string equal to "Human" or "Mouse" determining the reference organism to be used. For "Human" and "Mouse" org.Hg.eg.db and org.Mm.eg.db will be used, respectively. If Org is not NULL, OrgDb must be NULL.
OrgDb The reference data base to be used. Use e.g. org.Ce.eg.db for 'Celegans' when analysing Celegans data. If OrgDb is not NULL, Org must be NULL.
outPath A file path where results will be saved.
pvalueCutoff A numerical value that determines a cutoff of adjusted pValue.
pAdjustMethod A string passed to the clusterProfiler::enrichGO function to determine the method for adjusting the p-value. Options include "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none".
fontSize A numerical value that determines the font size of the y-axis and the title in the plot.
verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.

Value

A list:
enriched A list of output of enrichment analysis for different database analyzed.
noEnrichment A vector of database names in which no enriched pathways were found.

The output is saved for each selected module under the moduleName_enrichment folder. There is a subfolder that includes an excel file and plot(s). Each sheet in the excel file corresponds to a pathway database (KEGG in the below example). Each row is an overrepresented pathway.

Author(s)

Isha Mehta, Habil Zare, and Sogand Sajedi

References

Guangchuang Yu, Li-Gen Wang, Yanyan Han and Qing-Yu He, clusterProfiler: an R package for comparing biological themes among gene clusters. OMICS: A Journal of Integrative Biology 2012, 16(5):284-287

**get.fitted.leaf**

Returns the leaf for each sample

**Description**

Taking as input a tree and data, this function determines the leaf each sample will fall in.

**Usage**

```r
get.fitted.leaf(c5Tree, inpDTemp, epsi = 10^(-7))
```

**Arguments**

- **c5Tree**: A decision tree of class C50 that uses module eigengenes, or NULL. If NULL, expression plots for all modules are created.
- **inpDTemp**: The possibly new data matrix with samples on rows
- **epsi**: A small perturbation to resolve the boundary issue

**Value**

A numeric vector of node indices named by samples (rows of inpDTemp)

**Note**

This function is tricky because C50 uses a global variable.

**Author(s)**

Amir Foroushani

**See Also**

enrichGO, enrichKEGG, enrichNCG, enrichPathway

---

**Examples**

```r
library(org.Hs.eg.db)
genes <- c("NM_170730", "NM_001013580", "NM_002142", "NM_003417", "NM_000082", "NM_006158", "NM_006047", "NM_022356", "NM_003979", "NM_001030", "NM_022872")
pl <- get.enriched.pw(genes=genes, idType="REFSEQ", pathwayDb="GO", Org="Human", outPath=getwd(), verbose=1)
```

---

**See Also**

Pigengene-package, make.decision.tree, compact.tree, compute.pigengene, module.heatmap, get.used.features, preds.at
get.genes

Examples

```r
## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml, mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1, saveDir="trees", minPerLeaf=15, doHeat=FALSE, verbose=3, toCompact=FALSE)
f1 <- get.fitted.leaf(c5Tree=trees$c5Trees[['15']], inpDTemp=pigengene$eigengenes)
```

get.genes

List the (most relevant) genes for a decision tree.

Description

This function returns all genes that are left after shrinking (compacting) a given tree. If enhance is set to TRUE, it makes sure that the output contains at least two genes from each used module.

Usage

```r
get.genes(c5Tree = NULL, pigengene = NULL, queue = NULL, modules = NULL, pos=0, enhance = TRUE)
```

Arguments

- `queue`: A character vector. The membership queue for a decision tree.
- `pos`: Number of genes that are considered from removal. Same interpretation as in `preds.at`
- `enhance`: If enhance is set to TRUE, the function makes sure that the output contains at least two genes from each used module. Otherwise, exactly the `pos` first elements of the queue are removed from consideration.
- `modules`: Named character vector listing the module assignments.
- `c5Tree`: A decision tree of class C50.
- `pigengene`: An object in `pigengene-class`, usually created by `compute.pigengene`.

Details

This function needs `modules` and `queue`, or alternatively, `c5Tree` and `pigengene`.

Value

A character vector containing the names of the genes involved in the modules whose eigengenes are used in the tree. If `pos > 0`, the first `pos` such genes with lowest absolute membership in their respective modules are filtered.
get.used.features

See Also

Pigengene-package.comact.tree, preds.at, get.used.features, make.decision.tree

Examples

```r
## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml, mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1, saveDir="trees", minPerLeaf=15, doHeat=FALSE, verbose=3, toCompact=FALSE)
g1 <- get.genes(c5Tree=trees$c5Trees[["15"]], pigengene=pigengene)
```

get.used.features  

Return the features used in a tree

Description

Only some of the features will be automatically selected and used in a decision tree. However, an object of class C5.0 does not have the selected feature names explicitly. This function parses the tree component and extracts the names of features contributing to the tree.

Usage

`get.used.features(c5Tree)`

Arguments

c5Tree  

A decision tree of class C5

Value

A character vector of the names of features (module eigengenes) contributing to the input decision tree.

Author(s)

Amir Foroushani

See Also

Pigengene-package, make.decision.tree, compact.tree, compute.pigengene, module.heatmap, get.fitted.leaf, preds.at, Pigengene-package
learn.bn

## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml, mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1,
    saveDir="trees", minPerLeaf=15, doHeat=FALSE, verbose=3,
    toCompact=FALSE)
get.used.features(c5Tree=trees$c5Trees["15"])

---

learn.bn  

### Description

This function takes as input the eigengenes of all modules and learns a Bayesian network using bnlearn package. It builds several individual networks from random starting networks by optimizing their score. Then, it infers a consensus network from the ones with relatively "higher" scores. The default hyper-parameters and arguments should be fine for most applications.

### Usage

```r
learn.bn(pigengene=NULL, Data=NULL, Labels=NULL, bnPath = "bn", bnNum = 100,
    consensusRatio = 1/3, consensusThresh = "Auto", doME0 = FALSE,
    selectedFeatures = NULL, trainingCases = "All", algo = "hc",
    scoring = "bde", restart = 0, pertFrac = 0.1, doShuffle = TRUE,
    use.Hartemink = TRUE, bnStartFile = "None", use.Disease = TRUE,
    use.Effect = FALSE, dummies = NULL,
    tasks = "All", onCluster = !(which.cluster()$cluster == "local"),
    inds = 1:ceiling(bnNum/perJob), perJob = 2, maxSeconds = 5 * 60,
    timeJob = "00:10:00", bnCalculationJob = NULL, seed = NULL,
    verbose = 0, naTolerance=0.05)
```

### Arguments

- **pigengene**: An object from `pigengene-class`. The output of `compute.pigengene` function.
- **Data**: A matrix or data frame containing the training data with eigengenes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
- **Labels**: A (preferably named) vector containing the Labels (condition types) for the training data. Names must agree with rows of `Data`.
- **bnPath**: The path to save the results.
bnNum | The total number of individual networks. In practice, the number of learnt networks can be less than bnNum because some jobs may take too long and be terminated.

consensusRatio | A numeric in the range 0-1 that determines what portion of highly scored networks should be used to build the consensus network.

consensusThresh | A vector of thresholds in the range 0-1. For each threshold t, a consensus network will be build by considering the arcs that are present in at least a fraction of t of the individual networks. Alternatively, if it is "Auto" (the default), the threshold will be automatically set to the mean plus the standard deviation of the frequencies (strengths) of all arcs in the individual networks.

doME0 | If TRUE, module 0 (the outliers) will be considered in learning the Bayesian network.

selectedFeatures | A character vector. If not NULL, only these features (eigengenes) will be used.

trainingCases | A character vector that determines which cases (samples) should be considered for learning the network.

algo | The algorithm that bnlearn uses for optimizing the score. The default is "hc" (hill climbing). See arc.strength for other options and more details.

scoring | A character determining the scoring criteria. Use 'bde' and 'bic' for the Bayesian Dirichlet equivalent and Bayesian Information Criterion scores, respectively. See score for technical details.

restart | The number of random restarts. For technical use only. See hc.

pertFrac | A numeric in the range 0-1 that determines the number of attempts to randomly insert/remove/reverse an arc on every random restart. For technical use only.

doShuffle | The ordering of the features (eigengenes) is important in making the initial network. If doShuffle=TRUE, they will be shuffled before making every initial network.

use.Hartemink | If TRUE, Hartemink algorithm will be used to discretize data. Otherwise, interval discretization will be applied. See bnlearn:discretize.

bnStartFile | Optionally, learning can start from a Bayesian network instead of a random network. bnStartFile should contain a list called selected and selected$BN should be an object of bn-class. Non-technical users can set to "None" to disable.

use.Disease | If TRUE, the condition variable Disease will be included in the network, which cannot be the child of any other variable.

use.Effect | If TRUE, the condition variable beAML will be included in the network, which cannot be the parent of any other variable.

dummies | A vector of numeric values in the range 0-1. Dummy random variables will be added to the Bayesian network to check whether the learning process is effective. For development purposes only.

tasks | A character vector and a subset of c("learn","harvest","consensus","graph") that identifies the tasks to be done. Useful if part of the analysis was done previously, otherwise set to "All".
onCluster A Boolean variable that is FALSE if the learning is not done on a computer cluster.

inds The indices of the jobs that are included in the analysis.

perJob The number of individual networks that are learnt by 1 job.

maxSeconds An integer limiting computation time for each training job that runs locally, i.e., when oncluster=FALSE.

timeJob The time in "hh:mm:ss" format requested for each job if they are running on a computer cluster.

bnCalculationJob A script used to submit jobs to the cluster. Set to NULL if not using a cluster.

seed The random seed that can be set to an integer to reproduce the same results.

verbose Integer level of verbosity. 0 means silent and higher values produce more details of computation.

naTolerance Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See check.pigengene.input.

Details

For learning a Bayesian network with tens of nodes (eigengenes), bnNum=1000 or higher is recommended. Increasing consensusThresh generally results in a network with fewer arcs. Nagarajan et al. proposed a fundamental approach that determines this hyper-parameter based on the background noise. They use non-parametric bootstrapping, which is not implemented in the current package yet. The default values for the rest of the hyper-parameters should be fine for most applications.

Value

A list of:

- consensusThresh The vector of thresholds as described in the arguments.
- indvPath The path where the individual networks were saved.
- moduleFile The file containing data in appropriate format for bnlearn package and the blacklist arcs.
- scoreFile The file containing the record of the successively jobs and the scores of the corresponding individual networks.
- consensusFile The file containing the consensus network and its BDe and BIC scores.
- bnModuleRes The result of bn.module function. Useful mostly for development.
- runs A list containing the record of successful jobs.
- scores The list saved in scoreFile.
- consensusThreshRes The full output of consensus.thresh() function.
- consensus1 The consensus Bayesian network corresponding to the first threshold. It is the output of consensus function and consensus1$BN is an object of bn-class.
scorePlot The output of plot.scores function, containing the scores of individual networks.

graphs The output of plot.graphs function, containing the BDe score of the consensus network.

timeTaken An object of difftime-class recording the learning wall-time.

use.Disease, use.Effect, use.Hartemink Some of the input arguments.

Note
Running the jobs on a cluster needs bnCalculationJob script, which is NOT included in the package yet.

Author(s)
Amir Foroushani, Habil Zare, and Rupesh Agrahari

References


See Also
bnlearn-package, Pigengene-package, compute.pigengene

Examples
data(eigengenes33)
ms <- 10:20 ## A subset of modules for quick demonstration
amlE <- eigengenes33$aml[,ms]
mdsE <- eigengenes33$mds[,ms]
eigengenes <- rbind(amlE, mdsE)
Labels <- c(rep("AML", nrow(amlE)), rep("MDS", nrow(mdsE)))
names(Labels) <- rownames(eigengenes)
learnt <- learn.bn(Data=eigengenes, Labels=Labels, bnPath="bnExample", bnNum=10, seed=1)
bn <- learnt$consensus1$BN

## Visualize:
d1 <- draw.bn(BN=bn, nodeFontSize=14)

## What are the children of the Disease node?
childrenD <- bnlearn::children(x=bn, node="Disease")
print(childrenD)

## Fit the parameters of the Bayesian network:
fit <- bnlearn::bn.fit(x=bn, data=learnt$consensus1$Data, method="bayes", iss=10)

## The conditional probability table for a child of the Disease node:
fit[[childrenD[1]]]

## The fitted Bayesian network can be used for predicting the labels
## (i.e., values of the Disease node).
l2 <- predict(object=fit, node="Disease", data=learnt$consensus1$Data, method="bayes-lw")
table(Labels, l2)

---

**make.decision.tree**  
_Creates a decision tree to classify samples using the eigengenes values_

### Description
A decision tree in Pigengene-package uses module eigengenes to build a classifier that distinguishes the different classes. Briefly, each eigengene is a weighted average of the expression of all genes in the module, where the weight of each gene corresponds to its membership in the module.

### Usage

```
make.decision.tree(pigengene, Data,  
Labels = structure(pigengene$annotation[rownames(pigengene$eigengenes), 1], names = rownames(pigengene$eigengenes)),
  testD = NULL, testL = NULL, selectedFeatures = NULL,
  saveDir = "C5Trees", minPerLeaf = NULL, useMod0 = FALSE,
  costRatio = 1, toCompact = NULL, noise = 0, noiseRepNum = 10, doHeat=TRUE,
  verbose = 0, naTolerance=0.05)
```

### Arguments

- **pigengene**  
The pigengene object that is used to build the decision tree. See pigengene-class.

- **Data**  
The training expression data

- **Labels**  
Labels (condition types) for the (training) expression data. It is a named vector of characters. Data and pigengene will be subset according to these names.

- **testD**  
The test expression data, for example, from an independent dataset. Optional.

- **testL**  
Labels (condition types) for the (test) expression data. Optional.

- **selectedFeatures**  
A numeric vector determining the subset of eigengenes that should be used as potential predictors. By default ("All"), eigengenes for all modules are considered. See also useMod0.

- **saveDir**  
Where to save the plots of the tree(s).

- **minPerLeaf**  
Vector of integers. For each value, a tree will be built requiring at least that many nodes on each leaf. By default (NULL), several trees are built, one for each possible value between 2 and 10 percent of the number of samples.
useMod0: Boolean. Whether to allow the tree(s) to use the eigengene of module 0, which corresponds to the set of outliers, as a proper predictor.

costRatio: A numeric value effective only for 2 groups classification. The default value (1) considers the misclassification of both conditions as equally disadvantageous. Change this value to a larger or smaller value if you are more interested in the specificity of predictions for condition 1 or condition 2, respectively.

toCompact: An integer. The tree with this minPerLeaf value will be compacted (shrunk). Compacting in this context means reducing the number of required genes for the calculation of the relevant eigengenes and making the predictions using the tree. If NULL (default), the (presumably) most general proper tree (corresponding to the largest value in the minPerLeaf vector for which a tree could be constructed) is compacted. Set to FALSE to turn off compacting.

noise, noiseRepNum: For development purposes only. These parameters allow investigating the effect of gaussian noise in the expression data on the accuracy of the tree for test data.

doHeat: Boolean. Set to FALSE not to plot the heatmaps for faster computation.

verbose: The integer level of verbosity. 0 means silent and higher values produce more details of computation.

naTolerance: Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See check.pigengene.input.

Details

This function passes the input eigengenes and appropriate arguments C5.0 function from C50 package.

Value

A list with following elements:

call: The call that created the results

c5Trees: A list, with one element of class C5.0 for each attempted minNodesperleaf value. The list is named with the corresponding values as characters.

minPerLeaf: A numeric vector enumerating all of the attempted minPerLeaf values.

compacted: The full output of compact.tree function if toCompact is not FALSE

heat: The output of module.heatmap function for the full tree if doHeat is not FALSE

heatCompact: The output of module.heatmap function for the compacted tree if toCompact is not FALSE

noisy: The full output of noise.analysiy function if noise is not 0. For development and evaluation purposes only.

leafLocs: A matrix reporting the leaf for each sample on 1 row. The columns are named according to the corresponding minNodesperleaf value.

toCompact: Echoes the toCompact input argument

costs: The cost matrix

saveDir: The directory where plots are saved in
Note

For faster computation in an initial, explanatory run, turn off compacting, which can take a few minutes, with toCompact=FALSE.

See Also

Pigengene-package, compute.pigengene, compact.tree, C5.0, Pigengene-package

Examples

```r
## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml, mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1,
                               saveDir="trees", minPerLeaf=14:15, doHeat=FALSE, verbose=3,
                               toCompact=15)
```

make.filter  Computes the filter based on a similarity network

Description

Takes as input the similarity matrix of a graph (i.e., network) and an epsilon value. It computes a filter graph using the epsilon threshold. The dimension of the output filter matrix is the same as the input similarity network. It also produces two plots showing the weighted degrees of the input graph and degrees of the filter, respectively.

Usage

```r
make.filter(network, epsilon, outPath=NULL)
```

Arguments

- `network`: A matrix of similarity for the network.
- `epsilon`: A threshold for deciding which edges to keep. If the similarity is less than 1/epsilon (i.e., distance > epsilon), the edge will be removed, and it will be kept in the filter graph otherwise.
- `outPath`: A string determining the path where plots and results will be saved.
Description

Gene expression profile of 164 myelodysplastic syndromes (MDS) cases from Mills et al. study. The profile was compared with the profile of 202 acute myeloid leukemia (AML) cases and only the 1000 most differentially expressed genes are included.

Usage

data("mds")

Format

A numeric matrix
Details
The columns and rows are named according to the genes Entrez, and patient IDs, respectively. The original data was produced using Affymetrix Human Genome U133 Plus 2.0 Microarray. Mills et al. study is part of the MILE Study (Microarray Innovations In LEukemia) program, and aimed at prediction of AML transformation in MDS.

Value
It is a 164*1000 numeric matrix.

Note
This profile includes data of the 25 chronic myelomonocytic leukemia (CMLL) cases that can have different expression signatures according to Mills et al.

Source

References

See Also
Pigengene-package, one.step.pigengene, aml, compute.pigengene

Examples
library(pheatmap)
data(mds)
pheatmap(mds[,1:20],show_rownames=FALSE)

message.if
Conditional messaging.

Description
Messages only if verbose is more than 0 and write in a text file if provided.

Usage
message.if(me=NULL, verbose=0, txtFile=NULL, append=TRUE, ...)

module.heatmap

Arguments

me  The Message. Can be a character vector.
verbose  A integer.
txtFile  The text file in which the message will be written. Set to NULL to disable.
append  logical. Set to FALSE to overwrite txtFile.
...  Arguments to be passed to capture.output.

Value

NULL

Author(s)

Amir Foroushani

Examples

message.if("Hello world!", verbose=1)

module.heatmap

Plots heatmaps for modules

Description

This function takes as input a tree and an object from pigengene-class and per any module used in the tree, it plots one gene expression heatmap. Alternatively, it can plot a heatmap for every module in the given pigengene object.

Usage

module.heatmap(c5Tree=NULL, pigengene, mes=NULL, saveDir, testD = NULL, testL = NULL, pos = 0, verbose=0, doAddEigengene=TRUE, scalePngs=1, ...)

Arguments

c5Tree  A decision tree of class C50 that uses module eigengenes, or NULL. If NULL, expression plots for all modules are created.
pigengene  A object of pigengene-class, output of compute.pigengene
mes  A character vector that determines which modules to plot, e.g., c("ME3","ME5"). Set it to NULL to plot a heatmap for every module. This argument will be ignored if c5Tree is not NULL.
saveDir  Directory to save the plots
testD, testL  Optional. The matrix of (independent) test expression data, and the corresponding vector of labels. testL must be named according to the row names of testD.
one.step.pigengene

pos Number of genes to discard. Interpreted the same way as in compact.tree and preds.at
verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.
doAddEigengene If TRUE, the eigengene of each module will be added to the corresponding heatmap.
scalePngs If not 1, the size of pngs will be adjusted using this parameter. A typical value would be 7.
... Additional arguments. Passed to pheatmap.type

Value

A list of:
call The call that created the results
saveDir An echo of the input argument determining where the plots are saved

See Also

Pigengene-package, make.decision.tree, compact.tree, compute.pigengene

Examples

## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml,mds)

## Plotting the heatmaps of all modules:
module.heatmap(pigengene=pigengene, saveDir="heatmaps", pos=0, verbose=1)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1,  
  saveDir="trees", minPerLeaf=14:15, doHeat=FALSE, verbose=3,  
  toCompact=15)

## Plotting the heatmaps of only the modules in the tree:
module.heatmap(c5Tree=trees$c5Trees[["15"]], pigengene=pigengene,  
  saveDir="treeHeatmaps", pos=0, verbose=1)

---

one.step.pigengene  Runs the entire Pigengene pipeline

Description

Runs the entire Pigengene pipeline, from gene expression to compact decision trees in a single function. It identifies the gene modules using coexpression network analysis, computes eigengenes, learns a Bayesian network, fits decision trees, and compact them.
Usage

one.step.pigengene(Data, saveDir="Pigengene", Labels, testD=NULL, testLabels=NULL, doBalance=TRUE, RsquaredCut=0.8, costRatio=1, toCompact=FALSE, bnNum=0, bnArgs=NULL, useMod0=FALSE, mit="All", verbose=0, doHeat=TRUE, seed=NULL, doNetOnly=FALSE, doReturnNetworks=doNetOnly, idType="ENTREZID", pathwayDb=NULL, OrgDb=org.Hs.eg.db)

Arguments

Data A matrix or data frame (or list of matrices or data frames) containing the training expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named. For example, from RNA-Seq data, log(RPKM+1) can be used.

Labels A (preferably named) vector containing the Labels (condition types) for the training Data. Or, if Data is a list, a list of label vectors corresponding to the data sets in Data. Names must agree with rows of Data.

saveDir Directory to save the results.

testD Test expression data with syntax similar to Data, possibly with different rows and columns. This argument is optional and can be set to NULL if test data are not available.

testLabels A (preferably named) vector containing the Labels (condition types) for the test Data. This argument is optional and can be set to NULL if test data are not available.

doBalance Boolean. Whether the data should be oversampled before identifying the modules so that each condition contribute roughly the same number of samples to clustering.

RsquaredCut A threshold in the range [0,1] used to estimate the power. A higher value can increase power. For technical use only. See pickSoftThreshold for more details. A larger value generally leads to more modules.

costRatio A numeric value, the relative cost of misclassifying a sample from the first condition vs. misclassifying a sample from the second condition.

toCompact An integer value determining which decision tree to shrink. It is the minimum number of genes per leaf imposed when fitting the tree. Set to FALSE to skip compacting, to NULL to automatically select the maximum value.

bnNum Desired number of bootstrapped Bayesian networks. Set to 0 to skip BN learning.

bnArgs A list of arguments passed to learn.bn function.

useMod0 Boolean, whether to allow module zero (the set of outliers) to be used as a predictor in the decision tree(s).

mit The "module identification type", a character vector determining the reference conditions for clustering. If 'All' (default), clustering is performed using the entire data regardless of condition.

verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.
doHeat If TRUE the heatmap of expression of genes in the modules that contribute to the
tree will be plotted.

seed Random seed to ensure reproducibility.

d0rderByW If TRUE, the genes will be ordered in the csv file based on their absolute weight
in the corresponding module.

naTolerance Upper threshold on the fraction of entries per gene that can be missing. Genes
with a larger fraction of missing entries are ignored. For genes with smaller frac-
tion of NA entries, the missing values are imputed from their average expression
in the other samples. See check.pigengene.input.

doNetOnly If TRUE, the pipeline does not continue after making the network and identifying
the modules, e.g., eigengenes will not be computed.

doReturNetworks A boolean value to determine whether to return Network, which is relatively a
big matrix (typically GBs). Set to FALSE not to waste memory.

idType A string describing the type of input gene ID e.g., "ENTREZID", "REFSEQ",
"SYMBOL".

pathwayDb A character vector determining which enrichment database to be used by the
get.enriched.pw function e.g., "GO", "KEGG", "REACTOME", or "NCG".
Set to NULL to skip the pathway enrichment analysis.

OrgDb The reference data base to be used. Use e.g. org.Ce.eg.db for 'Celegans' when
analysing Celegans data. If OrgDb is not NULL, Org must be NULL.

Details
This is the main function of the package Pigengene and performs several steps: First, modules are
identified in the training expression data, according to mit argument i.e. based on coexpression
behaviour in the corresponding conditions. Set it to "All" to use all training data for this step
regardless of the condition. Then, if a list of data frames is provided in Data, similarity networks
on the data sets are computed and combined into one similarity network for the union of nodes
across data sets. Then, the eigengenes for each module and each sample are calculated, where the
expression of an eigengene of a module in a sample is the weighted average of the expression of the
genes in that module in the sample. Technically, an eigengene is the first principal component of
the gene expression in a module. PCA ensures that the maximum variance across all the training
samples is explained by the eigengene. Next, (optionally --if bnNum is set to a value greater than
0), several bootstrapped Bayesian networks are learned and combined into a consensus network, in
order to detect and illustrate the probabilistic dependencies between the eigengenes and the disease
subtype. Next, decision tree(s) are built that use the module eigengenes, or a subset of them, to
distinguish the classes (Labels). The accuracy of trees is assessed on the train and (if provided)
test data. Finally, the number of required genes for the calculation of the relevant eigengenes is
reduced (the tree is 'compacted'). The accuracy of the tree is reassessed after removal of each gene.
Along the way, several self explanatory directories, heatmaps and plots are created and stored under
saveDir.

Value
A list with the following components:
call
modules
wgRes
betaRes
pigengene
learnBn
selectedFeatures
c5treeRes

Note

The individual functions are exported to facilitate running the pipeline step-by-step in a customized way.

Author(s)

Amir Foroushani, Habil Zare, Rupesh Agrahari, and Meghan Short

References


See Also

check.pigengene.input, balance, calculate.beta, wgcna.one.step, compute.pigengene, learn.bn, make.decision.tree, blockwiseModules

Examples

library(org.Hs.eg.db)
data(aml)
data(mds)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
p1 <- one.step.pigengene(Data=d1, saveDir=".", bnNum=10, verbose=1, seed=1, Labels=Labels, toCompact=FALSE, doHeat=FALSE)
plot(p1$c5treeRes$c5Trees[["34"]])
pheatmap.type

Plots heatmap with clustering only within types.

Description

This function first performs hierarchical clustering on samples (rows of data) within each condition. Then, plots a heatmap without further clustering of rows.

Usage

pheatmap.type(Data, annRow, type = colnames(annRow)[1],
doTranspose=FALSE, conditions="Auto",...)

Arguments

- **Data**: A matrix with samples on rows and features (genes) on columns.
- **annRow**: A data frame with 1 column or more. Row names must be the same as row names of Data.
- **type**: The column of annRow used for determining the condition
- **doTranspose**: If TRUE, the matrix will be transposed for the final plot. E.g., if the genes are on the columns of Data, they will be shown on rows of the heatmap.
- **conditions**: A character vector that determines the conditions, and their order, to be included in the heatmap. By default ("Auto"), an alphabetical order of all available conditions in annRow will be used.
- **...**: Additional arguments passed to pheatmap function.

Value

A list of:

- **pheatmapS**: The results of pheatmap function for each condition
- **pheat**: The output of final pheatmap function applied on all data
- **ordering**: The ordering of the rows in the final heatmap
- **annRowAll**: The row annotation used in the final heatmap

Note

If type is not determined, by default the first column of annRow is used.

Author(s)

Habil Zare

See Also

eigengenes33
Examples

data(eigengenes33)
d1 <- eigengenes33$aml
d2 <- eigengenes33$mds
Disease <- c(rep("AML",nrow(d1)), rep("MDS",nrow(d2)))
Disease <- as.data.frame(Disease)
rownames(Disease) <- c(rownames(d1), rownames(d2))
p1 <- pheatmap.type(Data=rbind(d1,d2),annRow=Disease,show_rownames=FALSE)

pigengene

An object of class Pigengene

Description

This is a toy example object of class pigengene-class. It is used in examples of Pigengene-package. Gene expression profile of 202 acute myeloid leukemia (AML) cases from Mills et al. study. The profile was compared with the profile of 164 myelodysplastic syndromes (MDS) cases and only the 1000 most differentially expressed genes are included.

Usage

data("aml")

Format

An object of pigengene-class.

Details

The object is made using compute.pigengene function from aml and mds data as shown in the examples. The R CMD build --resave-data trick was used to reduce the size of saved object from 3.1 MB to 1.4 MB.

Value

It is an object of pigengene-class.

Source


References

pigengene-class

See Also

Pigengene-package, pigengene-class, one.step.pigengene, mds, aml, compute.pigengene

Examples

library(pheatmap)
data(pigengene)
plot(pigengene, fontsize=12)

## To reproduce:
data(aml)
data(mds)
data(eigengenes33)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
modules33 <- eigengenes33$modules[rownames(d1)]

## Computing:
computed <- compute.pigengene(Data=d1, Labels=Labels, modules=modules33,
   saveFile="pigengene.RData", doPlot=FALSE, verbose=3)
class(computed)
plot(computed, fontsize=12, main="Reproduced")

---

pigengene-class

The pigengene class

Description

A pigengene object holds the eigengenes, weights (memberships) and other related information.

Details

A object of class pigengene is the output of compute.pigengene function. It is a list containing at least the following components:

- **call** The call that created the results.
- **Reptimes** A named vector reporting the number of repeats for each condition in the oversampling process, which is done by the balance function.
- **eigenResults** A list including at least eigengenes and varExplained. If doWgcna=TRUE, then this list will be the full output of moduleEigengenes function with some fixes, e.g., we change eigengenes to a matrix, and use genes as its row names. Also, varExplained is named according to modules.
- **Data** The data matrix of gene expression.
- **Labels** A character vector giving the condition (type) for each sample (row of Data).
- **eigengenes** The matrix of eigengenes ordered based on selectedModules if provided. Rows correspond to samples.
- membership: The matrix of weights of genes (rows) in all modules (columns).
- orderedModules: The module assignment numeric vector named with genes and ordered based on module number.
- annotation: A data frame containing labeling information useful in plotting. It has a column named "Condition". Rows have sample names.
- saveFile: The file where the pigengene object is saved.
- weightsCsvFile: The file containing the weights in csv format. See `dOrderByW=TRUE`.
- weights: The weight matrix, which is also saved in csv format. It has more columns than membership but rows may be in a different order if `dOrderByW=TRUE`.
- heavyToLow: If `dOrderByW=TRUE`, this will be the ordering of genes according to the modules the belong to, where the genes in each module are ordered based on the absolute value of the weights in that module. Also, the genes in the csv file are in this order.

For 2 or more groups (conditions), additional (optional) components include:

- pvalues: A numeric matrix with columns "pValue", "FDR", and "Bonferroni". Rows correspond to modules. The null hypothesis is that the eigengene is expressed with the same distribution in all groups (conditions).
- log.pvalues: A data frame with 1 column containing the logarithm of Bonferroni-adjusted pvalues in base 10.

### See Also

`Pigengene-package`, `plot.pigengene`, `wgcna.one.step`, `compute.pigengene`, `learn.bn`, `make.decision.tree`

---

**plot.pigengene**

Plots and saves a pigengene object

---

**Description**

Plots a couple of heatmaps of expression of the eigengenes, weights (memberships), and so on. Saves the plots in png format.

**Usage**

```r
## S3 method for class 'pigengene'
plot(x, saveDir = NULL, DiseaseColors="Auto", fontsize = 35, doShowColnames = TRUE, fontsizeCol = 25, doClusterCols = ncol(pigengene$eigengenes) > 1, verbose = 2, doShowRownames = "Auto", pngfactor = max(2, ncol(pigengene$eigengenes)/16), do0Mem = FALSE, ...)
```
Arguments

- **x**: The object from `pigengene-class` computed by `compute.pigengene`.
- **saveDir**: The directory for saving the plots.
- **DiseaseColors**: A vector of characters determining color for each disease. Names should match the values in the first column of `x$annotation`.
- **fontsize**: Passed to `pheatmap.type`.
- **doShowColnames**: Boolean.
- **fontsizeCol**: Numeric.
- **doClusterCols**: Boolean.
- **verbose**: The integer level of verbosity. 0 means silent and higher values produce more details of computation.
- **doShowRownames**: Boolean.
- **pngfactor**: A numeric adjusting the size of the png files.
- **do0Mem**: If TRUE, module 0 genes are included in the membership heatmap.
- **...**: Passed to `pheatmap.type` function.

Details

Many of the arguments are passed to `pheatmap`.

Value

A list of:

- **heat**: The full output of `pheatmap` function
- **heatNotRows**: The full output of `pheatmap.type` function

Author(s)

Habil Zare ad Amir Foroushani

References


See Also

- `Pigengene-package`
- `compute.pigengene`
- `pheatmap.type`
## Data:
```r
data(aml)
data(mds)
data(eigengenes33)
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
Labels <- c(rep("AML", nrow(eigengenes33$aml)), rep("MDS", nrow(eigengenes33$mds)))
names(Labels) <- rownames(d1)
toyModules <- eigengenes33$modules[rownames(d1)]
```

## Computing:
```r
# Compute decision tree using Pigengene
p1 <- compute.pigengene(Data=d1, Labels=Labels, modules=toyModules,
                        saveFile="pigengene.RData", doPlot=TRUE, verbose=3)
plot(p1, saveDir="plots")
```

### preds.at

**Prediction using a possibly compacted tree**

**Description**

A decision tree in Pigengene uses module eigengenes to build a classifier that distinguishes two or more classes. Each eigengene is a weighted average of the expression of all genes in the module, where the weight of each gene corresponds to its membership in the module. Each module might contain dozens to hundreds of genes, and hence the final classifier might depend on the expression of a large number of genes. In practice, it can be desirable to reduce the number of necessary genes used by a decision tree. This function is helpful in observing changes to the classification output after removing genes with lower weights membership. It determines how a given decision tree would classify the expression data after removing a certain number of genes from consideration.

**Usage**

```r
preds.at(c5Tree, pigengene, pos=0, Data)
```

**Arguments**

- `c5Tree`: A decision tree that uses eigengenes from the pigengene object to classify the samples from the expression data.
- `pigengene`: A object of `pigengene-class`, output of `compute.pigengene`
- `pos`: Number of genes to be removed from the consideration. Genes are removed in ascending order of their absolute weight in the relevant modules. If 0 (default), the prediction will be done without compacting.
- `Data`: The expression possibly new data used for classification
Value

A list with following components:

- **predictions**: The vector of predictions after neglecting pos number of genes
- **eigengenes**: The values for the eigengenes after neglecting pos number of genes

See Also

Pigengene-package, pigengene-class, make.decision.tree, compact.tree, compute.pigengene, module.heatmap, get.used.features, get.fitted.leaf, Pigengene-package

Examples

```r
## Data:
data(aml)
data(mds)
data(pigengene)
d1 <- rbind(aml, mds)

## Fitting the trees:
trees <- make.decision.tree(pigengene=pigengene, Data=d1, saveDir="trees", minPerLeaf=15, doHeat=FALSE, verbose=3, toCompact=FALSE)
preds1 <- preds.at(c5Tree=trees$c5Trees[["15"]], pigengene=pigengene, pos=0, Data=d1)
```

---

**project.eigen**  
Infer eigengenes for given expression data

Description

This function projects (new) expression data onto the eigengenes of modules from another dataset. It is useful for comparing the expression behaviour of modules across (biologically related yet independent) datasets, for evaluating the performance of a classifier on new datasets, and for examining the robustness of a pattern with regards to missing genes.

Usage

```r
project.eigen(Data, saveFile = NULL, pigengene, naTolerance = 0.05, verbose = 0, ignoreModules = c())
```

Arguments

- **Data**: A matrix or data frame of expression data to be projected. Genes correspond to columns, and rows correspond to samples. Rows and columns must be named.
  It is OK to miss a few genes originally used to compute the eigengenes, thereby, projection is robust to choose of platform.
- **saveFile**: If not NULL, where to save the results in .RData format.
pigengene  An object of **pigengene-class**, usually created by **compute.pigengene**

naTolerance  Upper threshold on the fraction of entries per gene that can be missing. Genes with a larger fraction of missing entries are ignored. For genes with smaller fraction of NA entries, the missing values are imputed from their average expression in the other samples. See **check.pigengene.input**.

verbose  The integer level of verbosity. 0 means silent and higher values produce more details of computation.

ignoreModules  A vector of integers. In order to speed up the projection, it may be desirable to focus only on the eigengenes of a few interesting modules. In that case, the remaining modules can be listed here and will be ignored during projection (Optional).

Details

For each module, from the pigengene object, the weight (membership) of each gene is retrieved. The eigengene is computed (inferred) on the new data as a linear combination using the corresponding weights. The inferred eigengene vector will be normalized so that it has the same Euclidean norm as the original eigengene vector.

Value

A list of:

- **projected**  The matrix of inferred (projected) eigengenes
- **replacedNaNum**  The number of NA entries in the input Data that were replaced with the average expression of the corresponding gene
- **tooNaGenes**  A character vector of genes that were ignored because they had too many NAs
- **notMatched**  A character vector of genes in the original eigengene that could not be matched in the given input Data

Note

The new data should use the same type of biolocal identifiers (e.g. Gene Symbols or ENTREZIDs) as the original data for which the pigengene was constructed. It is, however, not required that the new data originate from the same type of technology, e.g. the eigengenes can be based on microarray experiments, whereas the new data comes from an RNA-Seq experiment. Nor is it necessary that the new dataset contains measurements for all of the genes from the original modules.

See Also

**Pigengene-package, compute.pigengene moduleEigengenes**

Examples

```r
# Data:
data(aml)
data(mds)
data(eigengenes33)
```
d1 <- rbind(aml, mds)
Labels <- c(rep("AML", nrow(aml)), rep("MDS", nrow(mds)))
names(Labels) <- rownames(d1)
toyModules <- eigengenes33$modules[colnames(d1)]
## Computing:
p1 <- compute.pigengene(Data=d1, Labels=Labels, modules=toyModules, saveFile="pigengene.RData", doPlot=TRUE, verbose=3)
## How robust projecting is?
p2 <- project.eigen(Data=d1, pigengene = p1, verbose = 1)
plot(p1$eigengenes[, "ME1"], p2$projected[, "ME1"])
stats::cor(p1$eigengenes[, "ME1"], p2$projected[, "ME1"])

---

**pvalues.manova**

*Computes pvalues for multi-class differential expression*

**Description**

Passes the arguments to `manova`, which performs multi-class analysis of variance.

**Usage**

`pvalues.manova(Data, Labels)`

**Arguments**

- **Data**: A matrix or data frame containing the (expression) data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
- **Labels**: A (preferably named) vector containing the Labels (condition types). Names must agree with rows of `Data`.

**Value**

A list with following elements:

- `call`: The call that created the results.
- `pvals`: The matrix of pvalues with columns "pValue", "FDR", "Bonferroni". Rows are named according to genes, the columns of `Data`.
- `manovaFit`: The full output of `manova` function.

**Note**

`oneway.test` function is a better generalization to Welch's t-test from 2-classes to multi-class because it does not assume that the variances are necessarily equal. However, in practice, with "enough number of samples", the two approaches will lead to similar p-values.
Author(s)

Amir Foroushani

References


B. L. Welch (1951), On the comparison of several mean values: an alternative approach.

See Also

oneway.test, manova, compute.pigengene

Examples

data(eigengenes33)
d1 <- rbind(eigengenes33$aml, eigengenes33$mds)
Labels <- c(rep("AML", nrow(eigengenes33$aml)), rep("MDS", nrow(eigengenes33$mds)))
names(Labels) <- rownames(d1)
ps <- pvalues.manova(Data=d1, Labels=Labels)
plot(log10(ps$pvals[, "Bonferroni"]))

---

save.if

Saves an object verbosely.

Description

Saves an R object, and reports the size of the saved object in memory and on file.

Usage

save.if(x1, file, compress=TRUE, verbose=1, ...)

Arguments

x1 The object to be saved.
file Where to save. If NULL, nothing will be saved.
compress A Boolean or character sent to the save function. The default TRUE leads to compression using gzip. With "xz", maximum compression is obtained in expense of more save and load time.
verbose A numeric determining how much detail will be printed.
... Optional arguments to be passed to the save function.

Value

A list including file, and a vector of sizes of the object in memory and on file.
wgcna.one.step

Author(s)
Amir Foroushani, and Habil Zare

See Also
message.if, save

Examples
m1 <- matrix(0, nrow=1000, ncol=1000)
save.if(m1, file="./m1.RData", verbose=3)

wgcna.one.step Module identification

Description
This function is a wrapper function for WGCNA::blockwiseModules and passes its arguments to it. Some other arguments are fixed.

Usage
wgcna.one.step(Data, power, saveDir=".", blockSize = "All", saveTOMs = FALSE, doThreads=FALSE, verbose = 0, seed = NULL)

Arguments
Data A matrix or data frame containing the expression data, with genes corresponding to columns and rows corresponding to samples. Rows and columns must be named.
power Soft-thresholding power for network construction
saveDir The directory to save the results and plots. NULL will disable saving.
blockSize The size of block when the data is too big. If not "All" (default) may introduce artifacts.
saveTOMs Boolean determining if the TOM data should be saved, which can be hundreds of MBs and useful for identifying hubs.
doThreads Boolean. Allows WGCNA to run a little faster using multi-threading but might not work on all systems.
verbose The integer level of verbosity. 0 means silent and higher values produce more details of computation.
seed Random seed to ensure reproducibility.

Details
Data, power, blockSize, saveTOMs, verbose, and seed are passed to WGCNA::blockwiseModules.
Value

A list with following components

- **call**: The command that created the results
- **genes**: The names of Data columns
- **modules**: A numeric vector, named by genes, that reports the module (clustering) assignments.
- **moduleColors**: A character vector, named by genes, that reports the color of each gene according to its module assignment
- **net**: The full output of `blockwiseModules` function
- **netFile**: The file in which the net object is saved
- **power**: An echo of the power argument.

References


See Also

- `blockwiseModules`, `pickSoftThreshold`, `calculate.beta`

Examples

data(aml)
wgRes <- wgcna.one.step(Data=aml[,1:200], seed=1, power=7,
  saveDir="wgcna", verbose=1)
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