Package ‘mAPKL’

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**Description** We propose a hybrid FS method (mAP-KL), which combines multiple hypothesis testing and affinity propagation (AP)-clustering algorithm along with the Krzanowski & Lai cluster quality index, to select a small yet informative subset of genes.

**License** GPL (&gt;= 2)

**biocViews** FeatureExtraction, DifferentialExpression, Microarray, GeneExpression

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A hybrid feature selection method for gene expression data

Description

A hybrid FS method (mAP-KL), which combines multiple hypothesis testing and affinity propagation (AP) clustering algorithm along with the Krzanowski & Lai cluster quality index, to select an informative subset of genes.

Details

Package: mAPKL
Type: Package
Version: 0.99.01
Date: 2014-05-07
License: GPL (>= 2)

Author(s)

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>

References


Annot-class

Class "Annot"

Description

S4 class for storing Annot analysis results

Slots

The following slots are defined for Annot objects:

- results: The accumulated annotation results
- probe: The probe id
- symbol: The official gene symbol
**entrezId**: The Entrez gene Identifier

**ensemblId**: The ensembl ID as indicated by ensembl

**map**: The cytoband locations of the gene

**Author(s)**

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>

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**annotate**  

*Genome annotation of the "exemplars".*

**Description**

The user may extract several genome specific information for the "exemplars" as described in the microarray annotation file.

**Usage**

`annotate(exemplars, chip)`

**Arguments**

- **exemplars**: The "exemplars" of the mAPKL class.
- **chip**: The platforms's name of the microarray chip used (e.g. "hgu133plus2.db")

**Details**

This function uses as key the probe id and returns the matching information as described in the gene chip annotation file. The returned information are usually multiple to the number of probe ids (one to many relationship).

**Value**

- **results**: The accumulated annotation results.
- **probe**: The probe id.
- **symbol**: The official gene symbol.
- **entrezId**: The Entrez gene Identifier.
- **ensemblId**: The ensembl ID as indicated by ensembl.
- **map**: The cytoband locations of the gene.

**Author(s)**

Argiris Sakellariou
Examples

```r
## We use the "exemplars" from the mAPKL.Rd example
exemplrs <- c(24, 26, 42, 45, 63, 81, 95, 99, 102, 113, 134, 135, 145, 152, 168)
names(exemplrs) <- c("215717_s_at", "1561358_at", "222752_s_at", "233922_at", "218871_x_at", "33323_r_at", "244311_at", "220932_at", "205508_at", "209596_at", "215180_at", "1560638_a_at", "201852_x_at", "229947_at", "221731_x_at")
gene.info <- annotate(exemplrs, "hgu133plus2.db")
```

classification

Classify samples according to the SVM algorithm

Description

This function performs classification through the Support Vector Machines (SVM) algorithm. The algorithm applies on the "exemplars" dataset. It produces a classification result either on the training set or on a validation set. This function estimates how well the selected "genes" from mAP-KL method discriminate between two phenotypes. The default SVM settings are: "linear" kernel and 5-folds cross-validation. Regarding the parameters for the "linear" kernel, cost parameter, and for the "radial" kernel, cost and gamma parameters, are estimated automatically through the `tune.svm` function as described in e1071 r-package.

Usage

```r
classification(trExemplObj, classLabels, valExemplObj=NULL, kf=5, kernel="linear")
```

Arguments

- `trExemplObj`: The exemplars train eSet object.
- `classLabels`: The varLabels name in the eSet object where the class labels are stored e.g "type".
- `valExemplObj`: The exemplars validation eSet object (if not NULL).
- `kf`: The k-folds value of the cross-validation parameter. The default value is 5-folds. By setting "Loo" or "LOO" a Leave-One-Out Cross Validation is performed.
- `kernel`: The type of kernel used for the classification analysis. The default kernel is "linear".

Value

- `classL`: The labels of the train set.
- `valClassL`: The labels of the validation set if not NULL.
- `predLbls`: The predicted labels according to the classification analysis.

Author(s)

Argiris Sakellariou
library(mAPKLData)
data(mAPKLData)
breast <- sampling(Data=mAPKLData, valPercent=40, classLabels="type", seed=135)
normTrainData <- preprocess(breast$trainData)
normTestData <- preprocess(breast$testData)

exprs(breast$trainData) <- normTrainData$clL2.normdata
exprs(breast$testData) <- normTestData$clL2.normdata

out.clL2 <- mAPKL(trObj=breast$trainData, classLabels="type", valObj=breast$testData, dataType=7)
clasPred <- classification(trExemplObj=out.clL2@exemplTrain, classLabels="type", valExemplObj=out.clL2@exemplTest)

### Classify-class

**Class “Classify”**

**Description**

S4 class for storing Classify analysis results

**Slots**

The following slots are defined for Classify objects:

- `classL`: Number of samples in the data set
- `valClassL`: Subset of samples used for leveraged clustering
- `predLbls`: Vector containing indices of exemplars
- `AUC`: The Area Under the ROC curve as a degree of samples discrimination
- `Accuracy`: The classification accuracy
- `MCC`: The MCC classification measure
- `Specificity`: The degree of true negative’s identification
- `Sensitivity`: The degree of true positive’s identification

**Author(s)**

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>
DataLD-class

Class "DataLD"

Description

S4 class for storing DataLD analysis results

Slots

The following slots are defined for DataLD objects:

- trainObj: An eSet class object of a training set
- valObj: An eSet class object of a validation set

Author(s)

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>

loadFiles

Imports gene expression data

Description

This function loads the train set, the class labels files as well as the test or validation file if any. Then we may perform normalization and (or) log2 transformation.

Usage

loadFiles(filesPath, trainFile, labelsFile, validationFile=NULL, validationLabels=NULL)

Arguments

- filesPath: The path where the files are stored
- trainFile: The genes and the relevant intensity values for feature selection analysis. The file should be of tab-delimited format
- labelsFile: The class labels of the samples
- validationFile: A further file with genes and intensity values used for validation purposes
- validationLabels: The class labels of the validation samples

Value

An object of Class DataLD

Author(s)

Argiris Sakellariou
The mAP-KL algorithm

Description

We first employ the mt.maxT function from the "multtest" package to rank the genes of the training set and then we reserve the top N genes (N = 200) for further exploitation. Prior to clustering analysis with Affinity Propagation we apply the index of Krzanowski and Lai as included in the "ClusterSim" package to determine the number of clusters solely on the disease samples of the training test set. The final step involves the cluster analysis with the AP clustering method as in the "apcluster" package, which detects n (n = k, the Krzanowski and Lai index) clusters among the top N genes and provides us with a list of the most representative genes of each cluster, the so called exemplars.

Usage

mAPKL(trObj, classLabels, valObj=NULL, dataType=6, statTest="t", permutations=1000, features=200, minClusters=2, maxClusters=50, FC="limma", bimaxit=50, r=2)

Arguments

- trObj: The train eSet object.
- classLabels: The varLabels name in the eSet object where the class labels are stored e.g "type".
- valObj: The validation eSet object (if not NULL).
- dataType: The type of the data e.g 6-ratio data without normalization and 7-interval or mixed (ratio & interval) data without normalization as described in "clusterSim" package.
- statTest: The statistical test applied to the geneIntensities. The available tests described in mt.maxT documentation in "multtest" package.
- permutations: The number of permutations.
- features: The top N genes to be kept.
- minClusters: The minimum number of clusters that can be identified.
- maxClusters: The maximum number of clusters that can be identified.
- FC: The Fold Change of the exemplars according to "Limma" (default). Alternatively the "SAM" approach may be computed.
- bimaxit: The maximum number of bisection steps performed by the AP algorithm. The (default) value is "50".
- r: The argument r is used to transform the resulting distances by computing the r-th power. To obtain negative squared distances as in Frey’s and Dueck’s(use r=2 as default).

Value

- rankedIntens: The top N ranked genes with their intensity values
- exemplTrain: The intensity values of the exemplars in the training set
- exemplTest: The intensity values of the exemplars in the validation set if not NULL
statistic  A list with the overall results of the "mt.maxT" analysis
adjp      The adjusted p-values according to the statistical analysis
pVal      The raw p-values according to the statistical analysis
fc         The Fold Change of the exemplars
exemplars The selected "significant" probe ids/genes
clusters  The probe ids/genes per cluster

Author(s)
Argiris Sakellariou

References

Examples
## Using separate train-test samples
## Load the necessary files based on Breast cancer data as included in the
## package mAPKLData
library(mAPKLData)
data(mAPKLData)
breast <- sampling(Data=mAPKLData, valPercent=40, classLabels="type", seed=135)
normTrainData <- preprocess(breast$trainData)
normTestData <- preprocess(breast$testData)
exprs(breast$trainData) <- normTrainData$clL2.normdata
exprs(breast$testData) <- normTestData$clL2.normdata
out.clL2 <- mAPKL(trObj=breast$trainData, classLabels="type",
valObj=breast$testData, dataType=7)

mAPKLRes-class  Class “mAPKLRes”

Description
S4 class for storing mAPKL analysis results

Slots
The following slots are defined for mAPKLRes objects:
rankedIntens: The top N ranked genes along with their intensity values
exemplTrain: An eSet class object formed with the exemplars of the training set
exemplTest: An eSet class object formed with the exemplars of the validation set if not NULL


**metrics**

statistic: A list with the overall results of the "mt.maxT" analysis
adjp: The adjusted p-values according to the statistical analysis
pVal: The raw p-values according to the statistical analysis
fc: The Fold Change of the exemplars
exemplars: The selected "significant" probe ids/genes
clusters: The probe ids/genes per cluster

**Author(s)**

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>

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**Description**

This function calculates several classification related metrics. It uses the original and the predicted samples' labels to quantify the quality of the classification process. Those measures give us a direct outlook of the selected "genes" and how well discriminate between two phenotypes.

**Usage**

metrics(classLbls, predLbls)

**Arguments**

classLbls The initial class labels.
predLbls The predicted class labels.

**Value**

AUC The Area Under the ROC curve as a degree of samples discrimination
Accuracy The classification accuracy
MCC The MCC classification measure
Specificity The degree of true negative's identification
Sensitivity The degree of true positive's identification

**Author(s)**

Argiris Sakellariou

**Examples**

```r
## Suppose 'val' represent the correct validation set labels
## and 'predictions' the predicted labels according to an SVM model
val <- c(rep(0,8),rep(1,4))
predictions <- c(rep(0,6),1,1,rep(1,3),0)
perfMetrics <- metrics(classLbls=val, predLbls=predictions)
```
### NetAttr-class

**Class**: "NetAttr"

**Description**

S4 class for storing some network characteristics of the top ranked genes

**Slots**

The following slots are defined for `NetAttr` objects:

- **edgelist**: The Node1 & Node2 & Weight edgelist matrix
- **degree**: The Local, Global and their Weighted values of the "degree" characteristic
- **closeness**: The Weighted values of the Local and Global "closeness" characteristic
- **betweenness**: The Weighted values of the Local and Global "betweenness" characteristic
- **transitivity**: The Weighted values of the Local and Global "transitivity" characteristic

**Author(s)**

Argiris Sakellariou <a.sakellariou@gonkhosp.gr>

---

### netwAttr

**Description**

Calculate some basic network characteristics of the top ranked genes

**Usage**

```r
netwAttr(mAPKLObj, net="clr")
```

**Arguments**

- **mAPKLObj**: An object of mAPKL class.
- **net**: The network reconstruction method to be employed. The user may select between "clr" (default), "aracne.a" and "aracne.m".

**Details**

It calculates some basic network characteristics. Those include the "degree", the "closeness", the "betweenness", and finally the "transitivity" or else clustering coefficient. We calculate the weighted values for both local and global scores.

The three available network reconstruction options are:
- **clr**: Context Likelihood or Relatedness Network
- **aracne.a**: Algorithm for the Reconstruction of Accurate Cellular Networks (additive model)
- **aracne.m**: Algorithm for the Reconstruction of Accurate Cellular Networks (multiplicative model)
Value

Upon successful completion, the function returns an `NetAttr` object.

Author(s)

Argiris Sakellariou

Examples

```r
library(mAPKLData)
data(mAPKLData)
breast <- sampling(Data=mAPKLData, valPercent=40, classLabels="type", seed=135)
normTrainData <- preprocess(breast$trainData)
normTestData <- preprocess(breast$testData)

exprs(breast$trainData) <- normTrainData$clL2.normdata
exprs(breast$testData) <- normTestData$clL2.normdata

out.clL2 <- mAPKL(trObj=breast$trainData, classLabels="type",
valObj=breast$testData, dataType=7)

net.attr <- netwAttr(mAPKLObj=out.clL2)
```

---

**preprocess**  
*Performs normalization and/or log2 transformation*

Description

This function performs normalization and/or log2 transformation on gene expression data.

Usage

```r
preprocess(exprsObj, log2=TRUE, norm="ALL", destname=NULL)
```

Arguments

- `exprsObj`: An eSet object where its assay data will be normalized
- `log2`: Performs logarithmic transformation of base 2 prior to any normalization. The default value is TRUE
- `norm`: The user may define a specific normalization method rather than "ALL" which is the default case. The available abbreviations are described in the details section
- `destname`: Here we define the destination path and the name of the jpeg file with the density plots. The default path is the working directory
Details

The available normalization methods are:
Mean-centering normalization "mc"
z-score normalization "z"
Quantile normalization "q"
Cyclic loess normalization "cl"
Mean-centering normalization and log2 transformation "mcL2"
z-score normalization and log2 transformation "zL2"
Quantile normalization and log2 transformation "qL2"
Cyclic loess normalization and log2 transformation "clL2"

Value

rawdata The initial gene expression values
mc.normdata The values after 'mean-centering' normalization
z.normdata The values after 'z-score' normalization
q.normdata The values after 'quantile' normalization
cl.normdata The values after 'cyclic loess' normalization
mcL2.normdata The values after 'mean-centering' normalization and log2
zL2.normdata The values after 'z-score' normalization and log2
qL2.normdata The values after 'quantile' normalization and log2
clL2.normdata The values after 'cyclic loess' normalization and log2

Author(s)

Argiris Sakellariou

Examples

library(mAPKLData)
data(mAPKLData)
varLabels(mAPKLData)
breast <- sampling(Data=mAPKLData, valPercent=40, classLabels="type", seed=135)
normTrainData <- preprocess(exprsObj=breast$trainData)

probes2pathways(annotObj)

Description

The user may extract the pathways where the "exemplars" are involved with the aid of the reactome database.

Usage

probes2pathways(annotObj)
Arguments
annotObj The "Annot" class object.

Details
This function utilizes the "Annot" class object as returned by the "annotate" function to extract the pathways where the "exemplars" are involved with the aid of the "reactome" database. We employ the probe Ids for the matching.

Author(s)
Argiris Sakellariou

Examples
## We use the "exemplars" from the mAPKL.Rd example
exemplrs <- c(24, 26, 42, 45, 63, 81, 95, 99, 102, 113, 134, 135, 145, 152, 168)
names(exemplrs)<- c("215717_s_at", "1561358_at", "222752_s_at", "233922_at", "218871_x_at", "23323_r_at", "244311_x_at", "220932_at", "209508_at", "209596_at", "215180_at", "1566638_a_at", "201852_x_at", "229947_at", "221731_x_at")
gene.info <- annotate(exemplrs,"hgu133plus2.db")

## We now use the "gene.info" to identify the relevant pathways
probes2pathways(gene.info)
Details

It presents the data samples with their phenotype labels, the exemplars with their statistical scores (adj.p-value, p-value and fc), and network characteristics (like weighted local degree, closeness, betweenness, transitivity) if such a network analysis has been performed. In addition, the report presents the classification performance achieved by those exemplars (either cross-validation or hold-out), and finally several annotation information (symbol, entrez id, ensemble id, and their chromosomal location) if an annotation analysis has been carried out.

Value

Upon successful completion an HTML report is saved in the working directory.

Author(s)

Argiris Sakellariou

Examples

```r
## When a network attributes object is present
## Not run: report(out,class.pred,class.metrics,netObj=net.attr, "C:/.../.../mAPKLreport.html")#Define a local path to store your report
## End(Not run)

## When an annotation object is present
## Not run: report(out,class.pred,class.metrics,gene.info, "C:/.../.../mAPKLreport.html")#Define a local path to store your report
## End(Not run)

## Without annotation and network attributes objects
## Not run: report(out,class.pred,class.metrics, file="C:/.../.../mAPKLreport.html")#Define a local path to store your report
## End(Not run)
```

---

**sampling**

*Splits a dataset to a train and a test sets of a user defined percentage*

Description

This function takes as input a dataset and splits it into a train and a test set based to a user defined percentage.

Usage

```r
sampling(Data,valPercent,classLabels,seed)
```

Arguments

- **Data**: The input dataset to be split as an eSet object.
- **valPercent**: The percentage of the input dataset used for validation purposes e.g. 40.
- **classLabels**: The varLabels name in the eSet object where the class labels are stored e.g "type".
- **seed**: Setting the seed number for reproducible sampling. The default value is 1.
Value

- `trainData` The data used for training as an eSet object
- `testData` The data used for validation as an eSet object

Author(s)

Argiris Sakellariou

Examples

```r
library(mAPKLDdata)
data(mAPKLDdata)
breast <- sampling(Data=mAPKLDdata, valPercent=40, classLabels="type", seed=135)
```
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