Package ‘PAC’

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Type Package

Title Partition-Assisted Clustering and Multiple Alignments of Networks

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Description Implements partition-assisted clustering and multiple alignments of networks. It 1) utilizes partition-assisted clustering to find robust and accurate clusters and 2) discovers coherent relationships of clusters across multiple samples. It is particularly useful for analyzing single-cell data set. Please see Li et al. (2017) <doi:10.1371/journal.pcbi.1005875> for detail method description.

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Imports Rcpp (>= 0.12.2), igraph, parmigene, infotheo, dplyr, Rtsne, ggplot2, ggrepel

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R topics documented:

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aggregateData

**Description**

Aggregates results from the clustering and merging step.

**Usage**

```r
aggregateData(dataInput, labelsInput)
```

**Arguments**

- `dataInput`: Data matrix, with first column being SampleID.
- `labelsInput`: Cluster labels from PAC.

**Value**

The aggregated data of `dataInput`, with average signal levels for all clusters and sample combinations.
### annotateClades

**Examples**

```r
n = 5e3  # number of observations
p = 1   # number of dimensions
K = 3   # number of clusters
w = rep(1,K)/K  # component weights
mu <- c(0,2,4)  # component means
ds <- rep(1,K)/K  # component standard deviations
g <- sample(1:K,prob=w,size=n,replace=TRUE)  # ground truth for clustering
X <- as.matrix(rnorm(n=n,mean=mu[g],sd=sd[g]))
y <- PAC(X, K)
X2<-as.matrix(rnorm(n=n,mean=mu[g],sd=sd[g]))
y2<-PAC(X2, K)
X<-cbind("Sample1", as.data.frame(X)); colnames(X)<-c("SampleID", "Value")
X2<-cbind("Sample2", as.data.frame(X2)); colnames(X2)<-c("SampleID", "Value")
aggregateData(rbind(X,X2),c(y,y2))
```

### Description

Creates annotation matrix for the clades in aggregated format. The matrix contains average signals of each dimension for each clade in each sample.

### Usage

```r
annotateClades(sampleIDs, topHubs)
```

### Arguments

- **sampleIDs**: sampleID vector
- **topHubs**: number of top ranked genes to output for annotation; annotation is a concatenated list of top ranked genes.

### Value

Annotated clade matrix
annotationMatrix_withSubpopProp

Adds subpopulation proportion for the annotation matrix for the clades

Description

Adds subpopulation proportion for the annotation matrix for the clades

Usage

annotationMatrix_withSubpopProp(aggregateMatrix_withAnnotation)

Arguments

aggregateMatrix_withAnnotation

the annotated clade matrix

Value

Annotated clade matrix with subpopulation proportions

BSPLLeaveCenter

Finds N Leaf centers in the data

Description

Finds N Leaf centers in the data

Usage

BSPLLeaveCenter(data, N = 40, method = "dsp")

Arguments

data a n x p data matrix

N number of leaves centers

method partition method, either "dsp (discrepancy based partition)", or "ll (bayesian sequential partition limited-look ahead)"

Value

leafctr N leaves centers
constellationPlot

*Description*

Makes constellation plot, in which the centroids are clusters are embedded in the t-SNE 2D plane and the cross-sample relationships are plotted as lines connecting related sample clusters (clades).

*Usage*

```r
constellationPlot(pacman_results, perplexity, max_iter, seed, plotTitle = "Constellations of Clades", nudge_x = 0.3, nudge_y = 0.3)
```

*Arguments*

- `pacman_results`: PAC-MAN analysis result matrix that contains network annotation, clade IDs and mean (centroid) clade expression levels.
- `perplexity`: perplexity setting for running t-SNE
- `max_iter`: max_iter setting for running t-SNE
- `seed`: set seed to make t-SNE and constellation plot to be reproducible
- `plotTitle`: max_iter setting for running t-SNE
- `nudge_x`: nudge on x coordinate of centroid labels
- `nudge_y`: nudge on y coordinate of centroid labels

---

fmeasure

*F-measure Calculation*

*Description*

Compute the F measure between the ground truth and the estimated label.

*Usage*

```r
fmeasure(g, t)
```

*Arguments*

- `g`: the ground truth
- `t`: estimated labels

*Value*

- `f`: the F measure
getAverageSpreadOf2SubpopClades

*Calculate the (global) average spread of subpopulations in clades with 2 subpopulations on the constellation plot.*

**Description**

Calculate the (global) average spread of subpopulations in clades with 2 subpopulations on the constellation plot.

**Usage**

```r
getAverageSpreadOf2SubpopClades(tsneResults, pacman_results)
```

**Arguments**

- `tsneResults`: t-SNE output of clade centroids’ embedding.
- `pacman_results`: PAC-MAN analysis result matrix that contains network annotation, clade IDs and mean (centroid) clade expression levels.

**Value**

Returns global average of 2-subpopulation clade spread on the constellation plot.

getExtraneousCladeSubpopulations

*Calculates subpopulations in clades (with two or more subpopulations) that are too far away from other subpopulations (within the same clade) on the constellation plot; these far away subpopulations should be pruned away from the original clades.*

**Description**

Calculates subpopulations in clades (with two or more subpopulations) that are too far away from other subpopulations (within the same clade) on the constellation plot; these far away subpopulations should be pruned away from the original clades.

**Usage**

```r
getExtraneousCladeSubpopulations(tsneResults, pacman_results, threshold_multiplier, max_threshold)
```
getRepresentativeNetworks

Arguments

**tsneResults**
- t-SNE output of clade centroids’ embedding.

**pacman_results**
- PAC-MAN analysis result matrix that contains network annotation, clade IDs and mean (centroid) clade expression levels.

**threshold_multiplier**
- how many times the threshold ( (a) spread from center of clade for clades with three or more sample subpopulations and (b) distance from each subpopulation centroid for clades with exactly two subpopulations).

**max_threshold**
- the maximum distance (on t-SNE plane) allowed for sample subpopulations to be categorized into the same clade.

Value

Returns clade subpopulations to be pruned.

Description

Outputs representative networks for clades/subpopulations larger than a size filter (very small subpopulations are not considered in downstream analyses)

Usage

```r
getRepresentativeNetworks(sampleIDs, dim_subset, SubpopSizeFilter, num_networkEdge)
```

Arguments

**sampleIDs**
- sampleID vector

**dim_subset**
- a string vector of string names to subset the data columns for PAC; set to NULL to use all columns

**SubpopSizeFilter**
- the cutoff for small subpopulations. Smaller subpopulations have unstable covariance structure, so no network structure is calculated

**num_networkEdge**
- the number of edges to draw for each subpopulation mutual information network
heatmapInput

Description

Creates the matrix that can be easily plotted with a heatmap function available in an R package

Usage

heatmapInput(aggregateMatrix_withAnnotation)

Arguments

aggregateMatrix_withAnnotation
the annotated clade matrix

Value

the heatmap input matrix

JaccardSM

Description

Calculates the Jaccard similarity matrix.

Usage

JaccardSM(network1, network2)

Arguments

network1    first network matrix input
network2    second network matrix input

Value

the alignment/co-occurrence score
MAN

*Creates network alignments using network constructed from subpopulations after PAC*

**Description**

Creates network alignments using network constructed from subpopulations after PAC

**Usage**

`MAN(sampleIDs, num_PACSupop, smallSubpopCutoff, k_clades)`

**Arguments**

- `sampleIDs`: sampleID vector
- `num_PACSupop`: number of subpopulations learned in PAC step for each sample
- `smallSubpopCutoff`: Population size cutoff for subpopulations in clade calculation. The small subpopulations will be considered in the refinement step.
- `k_clades`: number of clades to output before refinement

**Value**

`clades_network`: only the clades constructed without small subpopulations (by cutoff) using mutual information network alignments

**MINetworkPlot_topEdges**

*Plots mutual information network (mrnet algorithm) connection using the parmigene package. Mutual information calculated with infotheo package.*

**Description**

Plots mutual information network (mrnet algorithm) connection using the parmigene package. Mutual information calculated with infotheo package.

**Usage**

`MINetworkPlot_topEdges(dataMatrix, threshold)`

**Arguments**

- `dataMatrix`: data matrix
- `threshold`: the maximum number of edges to draw for each subpopulation mutual information network
MINetwork_matrix_topEdges

Mutual information network connection matrix generation (mrnet algorithm) using the parmigene package. Mutual information calculated with infotheo package.

Description

Mutual information network connection matrix generation (mrnet algorithm) using the parmigene package. Mutual information calculated with infotheo package.

Usage

MINetwork_matrix_topEdges(dataMatrix, threshold)

Arguments

dataMatrix

data matrix

threshold

the number of edges to draw for each subpopulation mutual information network

Value

the mutual information network connection matrix with top edges

MINetwork_simplified_topEdges

Outputs the vectorized summary of a network based on the number of edges connected to a node

Description

Outputs the vectorized summary of a network based on the number of edges connected to a node

Usage

MINetwork_simplified_topEdges(dataMatrix, threshold)

Arguments

dataMatrix

data matrix

threshold

the number of edges to draw for each subpopulation mutual information network
outputNetworks_topEdges_matrix

Wrapper to output the mutual information networks for subpopulations with size larger than a desired threshold.

Description

Wrapper to output the mutual information networks for subpopulations with size larger than a desired threshold.

Usage

outputNetworks_topEdges_matrix(dataMatrix, subpopulationLabels, threshold)

Arguments

dataMatrix data matrix with first column being the sample ID
subpopulationLabels the subpopulation labels
threshold the number of edges to draw for each subpopulation mutual information network

outputRepresentativeNetworks_topEdges

Outputs the representative/clade networks (plots and summary vectors) for subpopulations with size larger than a desired threshold. Saves the networks and the data matrices without the smaller subpopulations.

Description

Outputs the representative/clade networks (plots and summary vectors) for subpopulations with size larger than a desired threshold. Saves the networks and the data matrices without the smaller subpopulations.

Usage

outputRepresentativeNetworks_topEdges(dataMatrix, subpopulationLabels, threshold)

Arguments

dataMatrix data matrix with first column being the sample ID
subpopulationLabels the subpopulation labels
threshold the number of edges to draw for each subpopulation mutual information network
Partition Assisted Clustering (PAC) 1) utilizes dsp or bsp-ll to recursively partition the data space and 2) applies a short round of kmeans style postprocessing to efficiently output clustered labels of data points.

Description

Partition Assisted Clustering PAC 1) utilizes dsp or bsp-ll to recursively partition the data space and 2) applies a short round of kmeans style postprocessing to efficiently output clustered labels of data points.

Usage

PAC(data, K, maxlevel = 40, method = "dsp", max.iter = 50)

Arguments

data: a n x p data matrix
K: number of final clusters in the output
maxlevel: the maximum level of the partition
method: partition method, either "dsp(discrepancy based partition)", or "bsp(bayesian sequential partition)"
max.iter: maximum iteration for the kmeans step

Value

y cluster labels for the input

Examples

n = 5e3  # number of observations
p = 1   # number of dimensions
K = 3   # number of clusters
w = rep(1,K)/K  # component weights
mu <- c(0,2,4)  # component means
sd <- rep(1,K)/K  # component standard deviations
g <- sample(1:K,prob=w,size=n,replace=TRUE)  # ground truth for clustering
X <- as.matrix(rnorm(n=n,mean=mu[g],sd=sd[g]))
y <- PAC(X, K)
print(fmeasure(g,y))
recordWithinClusterSpread

*Calculates the within cluster spread*

**Description**

Calculates the within cluster spread

**Usage**

```r
recordWithinClusterSpread(sampleIDs, dim_subset = NULL, SubpopSizeFilter)
```

**Arguments**

- `sampleIDs`: A vector of sample names.
- `dim_subset`: a string vector of string names to subset the data columns for PAC; set to NULL to use all columns.
- `SubpopSizeFilter`: threshold to filter out very small clusters with too few points; these very small subpopulations may not be outliers and not biologically relevant.

**Value**

Returns the sample within cluster spread

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refineSubpopulationLabels

*Refines the subpopulation labels from PAC using network alignment and small subpopulation information. Outputs a new set of files containing the representative labels.*

**Description**

Refines the subpopulation labels from PAC using network alignment and small subpopulation information. Outputs a new set of files containing the representative labels.

**Usage**

```r
refineSubpopulationLabels(sampleIDs, dim_subset, clades_network_only, expressionGroupClamp)
```
renamePrunedSubpopulations

Description

Prune away specified subpopulations in clades that are far away.

Usage

renamePrunedSubpopulations(pacman_results, subpopulationsToPrune)

Arguments

pacman_results  PAC-MAN analysis result matrix that contains network annotation, clade IDs and mean (centroid) clade expression levels.

subpopulationsToPrune  A vector of clade IDs; these clades will be pruned.

Value

Returns PAC-MAN analysis result matrix with pruned clades. The pruning process creates new clades to replace the original clade ID of the specified subpopulations.
runElbowPointAnalysis Runs elbow point analysis to find the practical optimal number of clades to output. Outputs the average within sample cluster spread for all samples and the elbow point analysis plot with loess line fitted through the results.

Description

Runs elbow point analysis to find the practical optimal number of clades to output. Outputs the average within sample cluster spread for all samples and the elbow point analysis plot with loess line fitted through the results.

Usage

runElbowPointAnalysis(ks, sampleIDs, dim_subset, num_PACSupop, smallSubpopCutoff, expressionGroupClamp, SubpopSizeFilter)

Arguments

ks Vector that is a sequence of clade sizes.
sampleIDs A vector of sample names.
dim_subset a string vector of string names to subset the data columns for PAC; set to NULL to use all columns.
num_PACSupop Number of PAC subpopulation explored in each sample.
smallSubpopCutoff Cutoff of minor subpopulation not used in multiple alignments of networks
expressionGroupClamp clamps the subpopulations into desired number of expression groups for assigning small subpopulations into larger groups or their own groups.
SubpopSizeFilter threshold to filter out very small clusters with too few points in the calculation of cluster spreads; these very small subpopulations may be outliers and not biologically relevant.

samplePass Run PAC for Specified Samples

Description

A wrapper to run PAC and output subpopulation mutual information networks. Please use the PAC function itself for individual samples or if the MAN step is not needed.
Usage

samplePass(sampleIDs, dim_subset, hyperrectangles, num_PACSupop, max.iter, num_networkEdge)

Arguments

- **sampleIDs**: sampleID vector
- **dim_subset**: a string vector of string names to subset the data columns for PAC; set to NULL to use all columns
- **hyperrectangles**: number of hyperrectangles to learn for each sample
- **num_PACSupop**: number of subpopulations to output for each sample using PAC
- **max.iter**: postprocessing kmeans iterations
- **num_networkEdge**: a threshold on the number of edges to output for each subpopulation mutual information network
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