Package ‘MLP’

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Title Mean Log P Analysis
Type Package
Description Pathway analysis based on p-values associated to genes from a genes expression analysis of interest. Utility functions enable to extract pathways from the Gene Ontology Biological Process (GOBP), Molecular Function (GOMF) and Cellular Component (GOCC), Kyoto Encyclopedia of Genomes of Genomes (KEGG) and Reactome databases. Methodology, and helper functions to display the results as a table, barplot of pathway significance, Gene Ontology graph and pathway significance are available.

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### Description

Utility function which adds the biological description of the gene sets as a column to the return value of the MLP function (data frame)

### Usage

```
addGeneSetDescription(object, geneSetSource = NULL)
```

### Arguments

- **object**
  - object of class 'MLP' as produced by the 'MLP' function

- **geneSetSource**
  - source to be used to construct the list of pathway categories; for public data sources, the user can specify a string (one of 'GOBP', 'GOMF', 'GOCC', 'KEGG' or 'REACTOME') and BioC packages will be used to construct the list of pathway categories; for non-public data sources, the user can pass the pathway data as a dataframe with (at least) the following four columns: PATHWAYID, TAXID, PATHWAYNAME and GENEID. It is assumed all columns are of type character. The `geneSetSource` argument should be the same as the argument provided to the getGeneSets function; defaults to NULL
getGeneSets

Prepare Pathway Data for the MLP Function

Description

The return value of the getGeneSets function has as primary use to serve as geneSet argument for the MLP function

Usage

geneSet <- getGeneSets(species = "Mouse", geneSetSource = "GOBP", entrezIdentifiers = names(examplePValues))
mlp <- MLP(geneSet = geneSet, geneStatistic = examplePValues, addGeneSetDescription = FALSE)
head(mlp)

Arguments

- **species**: character vector of length one indicating the species, one of 'Mouse', 'Human', 'Rat', 'Dog' or 'Rhesus'; defaults to 'Mouse'.
- **geneSetSource**: source to be used to construct the list of pathway categories; for public data sources, the user can specify a string (one of 'GOBP', 'GOMF', 'GOCC', 'KEGG' or 'REACTOME') and BioC packages will be used to construct the list of pathway categories; for non-public data sources, the user can pass the pathway data as a dataframe with (at least) the following four columns: PATHWAYID, TAXID, PATHWAYNAME and GENEID. It is assumed all columns are of type character.
- **entrezIdentifiers**: Entrez Gene identifiers used to subset the relevant gene set
Value

object of class geneSetMLP which is essentially a named list of pathway categories.
Each list component is named with the pathway ID and contains a vector of Entrez Gene identifiers related to that particular pathway.
The object contains additionally the attributes:

• 'species' and 'geneSetSource': species and geneSetSource (as provided as input)
• 'descriptions': named character vector with pathway descriptions. The vector is named with the pathway ID.

Examples

if (require(GO.db) && require(org.Mm.eg.db)){
  pathExamplePValues <- system.file("exampleFiles", "examplePValues.rda", package = "MLP")
  load(pathExamplePValues)
  geneSet <- getGeneSets(species = "Mouse", geneSetSource = "GOBP", entrezIdentifiers = names(examplePValues)[seq_len(2000)])
  geneSet <- getGeneSets(species = "Mouse", geneSetSource = "KEGG", entrezIdentifiers = names(examplePValues)[seq_len(2000)])
}

MLP

This function calculates p-values for each gene set based on row permutations of the gene p values or column permutations of the expression matrix; the p values can be obtained either as individual gene set p values or p values based on smoothing across gene sets of similar size.

Description

This function calculates p-values for each gene set based on row permutations of the gene p values or column permutations of the expression matrix; the p values can be obtained either as individual gene set p values or p values based on smoothing across gene sets of similar size.

Usage

MLP(
  geneSet,
  geneStatistic,
  minGenes = 5,
  maxGenes = 100,
  rowPermutations = TRUE,
  nPermutations = 100,
  smoothPValues = TRUE,
  probabilityVector = c(0.5, 0.9, 0.95, 0.99, 0.999, 0.9999, 0.99999),
  df = 9,
  addGeneSetDescription = TRUE
)
Arguments

- **geneSet** is the input list of gene sets (components) and gene IDs (character vectors). A gene set can, for example, be a GO category with for each category Entrez Gene identifiers; The `getGeneSets` function can be used to construct the geneSet argument for different pathway sources.

- **geneStatistic** is either a named numeric vector (if `rowPermutations` is TRUE) or a numeric matrix of pvalues (if `rowPermutations` is FALSE). The names of the numeric vector or row names of the matrix should represent the gene IDs.

- **minGenes** minimum number of genes in a gene set for it to be considered (lower threshold for gene set size)

- **maxGenes** maximum number of genes in a gene set for it to be considered (upper threshold for gene set size)

- **rowPermutations** logical indicating whether to use row permutations (TRUE; default) or column permutations (FALSE)

- **nPermutations** is the number of simulations. By default 100 permutations are conducted.

- **smoothPValues** logical indicating whether one wants to calculate smoothed cut-off thresholds (TRUE; default) or not (FALSE).

- **probabilityVector** vector of quantiles at which p values for each gene set are desired

- **df** degrees of freedom for the smooth.spline function used in `getSmoothedPValues`

- **addGeneSetDescription** logical indicating whether a column with the gene set description be added to the output data frame; defaults to TRUE.

Value

data frame with four (or five) columns: `totalGeneSetSize`, `testedGeneSetSize`, `geneSetStatistic` and `geneSetPValue` and (if `addDescription` is set to TRUE) `geneSetDescription`; the rows of the data frame are ordered by ascending `geneSetPValue`.

References

Raghavan, Nandini et al. (2007). The high-level similarity of some disparate gene expression measures, Bioinformatics, 23, 22, 3032-3038.

Examples

```r
if (require(GO.db)){
  pathExampleGeneSet <- system.file("exampleFiles", "exampleGeneSet.rda", package = "MLP")
  pathExamplePValues <- system.file("exampleFiles", "examplePValues.rda", package = "MLP")
  load(pathExampleGeneSet)
  load(pathExamplePValues)
  head(examplePValues)
  head(exampleGeneSet)
  mlpResult <- MLP(geneSet = exampleGeneSet, geneStatistic = examplePValues)
  head(mlpResult)
}
```
mlpBarplot

Draw a Barplot for MLP Results

Description

Draw a Barplot for MLP Results

Usage

mlpBarplot(
  object,
  nRow = 20,
  barColors = NULL,
  main = NULL,
  ylab = "",
  cex = 1
)

Arguments

  object             object of class MLP
  nRow              number of rows of the MLP data frame to depict in the barplot; defaults to 20.
  barColors         vector of colors to use for the bars of the barplot; defaults to NULL; if NULL, three gray shades are used reflecting the proportion of tested genes of a gene set versus the total number of genes in a gene set. If the proportion exceeds 75%, the darkest shade is used; between 50 and 75% a moderately dark shade is used; below 50% a lighter gray shade is used.
  main              main title; if NULL (default) "Effect of the treatment on <geneSetSource> gene sets" will be used
  ylab              string with label for the y-axis
  cex               numeric, cex used in par

Value

the midpoints of all the bars are returned invisibly (using the conventions of barplot); an MLP-specific barplot is drawn to the current device;

See Also

barplot
Examples

```r
pathExampleMLPResult <- system.file("exampleFiles", "exampleMLPResult.rda", package = "MLP")
load(pathExampleMLPResult)
dev.new(width = 10, height = 10)
op <- par(mar = c(30, 10, 6, 2))
mlpBarplot(exampleMLPResult)
par(op)
```

plot.MLP  
Plot the Results of an MLP Run

Description

Plot the Results of an MLP Run

Usage

```r
## S3 method for class 'MLP'
plot(x, y = NULL, type = c("barplot", "GOgraph", "quantileCurves"), ...)
```

Arguments

- `x`: object of class 'MLP'
- `y`: argument added to comply with generic; not used, defaults to NULL
- `type`: character of length one; one of 'barplot', 'GOgraph' or 'quantileCurves'
- `...`: further arguments for the plot functions for each type

Value

for type = "barplot", the midpoints of the barplot

Examples

```r
pathExampleMLPResult <- system.file("exampleFiles", "exampleMLPResult.rda", package = "MLP")
load(pathExampleMLPResult)
dev.new(width = 10, height = 10)
op <- par(mar = c(30, 10, 6, 2))
plot(exampleMLPResult, type = "barplot")
par(op)
plot(exampleMLPResult, type = "quantileCurves")
if (require(GO.db) && require(Rgraphviz)){
  plot(exampleMLPResult, type = "GOgraph")
}
```
plotGeneSetSignificance

Plot the Significance for the Genes of a Given Gene Set

Description
Plot the Significance for the Genes of a Given Gene Set

Usage
plotGeneSetSignificance(
geneSet, geneSetIdentifier, geneStatistic, annotationPackage, barColors = NULL, descriptionInMainTitle = TRUE
)

Arguments

geneSet object of class 'geneSetMLP' as produced by function getGeneSets
geneSetIdentifier identifier of the gene set for which a significance plot should be produced; character of length one
geneStatistic named vector of gene statistics (e.g. p values); the names of the vector are Entrez Gene identifiers
annotationPackage name of the annotation package to be used (without .db extension); character of length one
barColors named vector of colors to use for the bars of the barplot; the names of the vector are Entrez Gene identifiers and the vector should be of length equal to the length of the geneStatistic vector defaults to NULL in which case 'grey50' is used
descriptionInMainTitle Boolean whether or not to use the gene set description in the main title of the plot

Value
no return value

Examples
pathExamplePValues <- system.file("exampleFiles", "examplePValues.rda", package = "MLP")
pathExampleGeneSet <- system.file("exampleFiles", "exampleGeneSet.rda", package = "MLP")
pathExampleMLPResult <- system.file("exampleFiles", "exampleMLPResult.rda", package = "MLP")
plotGOgraph

load(pathExampleGeneSet)
load(pathExamplePValues)
load(pathExampleMLPResult)

# annotationPackage <- if (require(mouse4302mmentrezg.db)) "mouse4302mmentrezg" else "mouse4302"
annotationPackage <- "mouse4302"
geneSetID <- rownames(exampleMLPResult)[1]
dev.new(width = 10, height = 10)
op <- par(mar = c(25, 10, 6, 2))
plotGeneSetSignificance(
    geneSet = exampleGeneSet,
    geneSetIdentifier = geneSetID,
    geneStatistic = examplePValues,
    annotationPackage = annotationPackage
)
par(op)

---

plotGOgraph  

Graphical Representation of GO Based MLP Results

Description

Graphical Representation of GO Based MLP Results

Usage

plotGOgraph(object, nRow = 5, main = NULL, nCutDescPath = 30)

Arguments

object  
object of class MLP (as produced by the MLP function)

nRow  
number of GO IDs for which to produce the plot

main  
main title of the graph; if NULL (default) the main title is set to ’GO graph’

nCutDescPath  
number of characters at which the pathway description should be cut (inserted in a new line), 30 by default

Value

GO graph is plotted to the current device

Examples

if (require(GO.db) && require(Rgraphviz)){
  pathExampleMLPResult <- system.file("exampleFiles", "exampleMLPResult.rda", package = "MLP")
  load(pathExampleMLPResult)
  plotGOgraph(exampleMLPResult, main = "GO Graph")
}
Index

addGeneSetDescription, 2
getGeneSets, 3, 5
MLP, 3, 4
mlpBarplot, 6
plot. MLP, 7
plotGeneSetSignificance, 8
plotGOgraph, 9