Package ‘EnrichDO’

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Type Package

Title a Global Weighted Model for Disease Ontology Enrichment Analysis

Version 1.7.0

Description To implement disease ontology (DO) enrichment analysis, this package is designed and presents a double weighted model based on the latest annotations of the human genome with DO terms, by integrating the DO graph topology on a global scale. This package exhibits high accuracy that it can identify more specific DO terms, which alleviates the over enriched problem. The package includes various statistical models and visualization schemes for discovering the associations between genes and diseases from biological big data.

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Contents

`EnrichDO-package` *EnrichDO Enrichment analyses including a variety of statistical models and visualization schemes for discovering the disease-gene relationship under biological big data.*

Description

To implement disease ontology (DO) enrichment analysis, this package is designed and presents a double weighted model based on the latest annotations of the human genome with DO terms, by integrating the DO graph topology on a global scale. This package exhibits high accuracy that it can identify more specific DO terms, which alleviates the over enriched problem. The package includes various statistical models and visualization schemes for discovering the associations between genes and diseases from biological big data.

Author(s)

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`convDraw` *convDraw*

Description

using the result of writeResult for convenience drawing.

Usage

```
convDraw(resultDO)
```

Arguments

`resultDO`	a data frame of enrichment result

Value

DataFrame

Author(s)

Haixiu Yang

Examples

```
#' #Draw from wrireResult output files
# Firstly, read the wrireResult output file,using the following two lines
data <- read.delim(file.path(system.file("examples", package = "EnrichDO"), "result.txt"))
enrich <- convDraw(resultDO = data)
# then, Use the drawing function you need
drawGraphViz(enrich = enrich) # Tree diagram
drawPointGraph(enrich = enrich) # Bubble diagram
drawBarGraph(enrich = enrich) # Bar plot
```

`doEnrich` *doEnrich*

Description

given an array of human protein-genes with NCBI ENTREZID format, this function combines topological properties of the disease ontology structure for enrichment analysis.

Usage

```
doEnrich(
  interestGenes,
 test = c("hypergeomTest", "fisherTest", "binomTest", "chisqTest", "logoddTest"),
 method = c("BH", "holm", "hochberg", "hommel", "bonferroni", "BY", "fdr", "none"),
  m = 1,
  maxGsize = 5000,
  minGsize = 5,
  traditional = FALSE,
  delta = 0.01,
  penalize = TRUE,
  allDOTerms = FALSE
)
```

Arguments

`interestGenes`	a vector of gene IDs.The interest gene sets should be protein-coding genes, using the ENTREZID format from NCBI.
`test`	One of 'fisherTest','hypergeomTest','binomTest','chisqTest' and 'logoddTest' statistical model. Default is hypergeomTest.

`method`	One of 'holm', 'hochberg', 'hommel', 'bonferroni', 'BH', 'BY','fdr' and 'none',for P value correction.
`m`	Set the maximum number of ancestor layers for ontology enrichment. Default is layer 1.
`maxGsize`	indicates that doterms with more annotation genes than maxGsize are ignored, and the P value of these doterms is set to 1.
`minGsize`	indicates that doterms with less annotation genes than minGsize are ignored, and the P value of these doterms is set to 1.
`traditional`	a logical variable, TRUE for traditional enrichment analysis, FALSE for enrichment analysis with weights. Default is FALSE.
`delta`	Set the threshold of nodes, if the p value of doterm is greater than delta, the nodes are not significant, and these nodes are not weighted.Default is 0.01.
`penalize`	Logical value, used to alleviate the impact of different magnitudes of p-values, default value is TRUE. When set to FALSE, the degree of reduction in weight for non-significant nodes is decreased.
`allDOTerms`	Logical value, whether to store all doterms in EnrichResult, defaults is FALSE (only significant nodes are retained).

Value

A `EnrichResult` instance.

Author(s)

Haixiu Yang

Examples

```
## Input data case
# the inputdata_demo variable stores validated protein-coding genes associated with Alzheimer's disease.
Alzheimer <- read.delim(file.path(system.file("extdata", package = "EnrichDO"), "Alzheimer_curated.csv"), hea
inputdata_demo <- Alzheimer[, 1]
## doEnrich case
# The enrichment results were obtained by using demo.data
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
demo_result <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
```

`dotermgenes` *All DO term annotated genes.*

Description

A dataset includes 15106 genes.

Usage

`dotermgenes`

Format

An character array with 15106 elements:

`doterms` *Detailed annotation information for 4831 DO terms.*

Description

A dataset includes 4831 DO terms of hierarchical information, annotated gene information, and weight information

Usage

```
doterms
```

Format

A data frame with 4813 rows and 10 variables:

DOID the DOterm ID on enrichment

level the hierarchy of the DOterm in the DAG graph

gene.arr all genes related to the DOterm

weight.arr gene weights in each node

parent.arr the parent node of the DOterm

parent.len the number of parent.arr

child.arr child nodes of the DOterm

child.len the number of child.arr

gene.len the number of all genes related to the DOterm

DOTerm the standard name of the DOterm

`drawBarGraph` *drawBarGraph*

Description

The enrichment results are shown in a bar chart

Usage

```
drawBarGraph(EnrichResult = NULL, enrich = NULL, n = 10, delta = 1e-15)
```

Arguments

`EnrichResult`	the EnrichResult object
`enrich`	a data frame of enrichment result
`n`	number of bars
`delta`	the threshold of P value

Value

bar graph

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
sample1 <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
drawBarGraph(EnrichResult = sample1, n = 10, delta = 0.05)
```

`drawGraphViz` *drawGraphViz*

Description

the enrichment results are shown in a tree diagram

Usage

```
drawGraphViz(
  EnrichResult = NULL,
  enrich = NULL,
  n = 10,
  labelfontsize = 14,
  numview = TRUE,
  pview = TRUE
)
```

Arguments

`EnrichResult`	the EnrichResult object
`enrich`	a data frame of the enrichment result
`n`	the number of most significant nodes
`labelfontsize`	the font size of nodes
`numview`	Displays the number of intersections between the interest set and each doterm.
`pview`	Displays the P value for each dotrem.

Value

tree diagram

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
sample5 <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
drawGraphViz(EnrichResult = sample5)

# The p-value and the number of intersections are not visible
drawGraphViz(EnrichResult = sample5, numview = FALSE, pview = FALSE)
```

`drawHeatmap` *drawHeatmap*

Description

The top DOID_n nodes in the enrichment results showed the top gene_n genes with the highest weight sum.

Usage

```
drawHeatmap(
  interestGenes,
  EnrichResult = NULL,
  DOID_n = 10,
  gene_n = 50,
  fontsize_row = 10,
  ...
)
```

Arguments

`interestGenes`	A collection of interest genes in vector form
`EnrichResult`	the EnrichResult object
`DOID_n`	There are DOID_n nodes with the highest significance in the enrichment results.
`gene_n`	Among the selected DOID_n nodes, the top gene_n genes with the highest weight sum are selected to show.
`fontsize_row`	Set the font size of the gene tag.
`...`	Other parameters in the pheatmap function also apply.

Value

heat map

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
sample6 <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
drawHeatmap(interestGenes = demo.data, EnrichResult = sample6, gene_n = 10)
```

`drawPointGraph` *drawPointGraph*

Description

The enrichment results are shown in a scatter plot

Usage

```
drawPointGraph(EnrichResult = NULL, enrich = NULL, n = 10, delta = 1e-15)
```

Arguments

`EnrichResult`	the EnrichResult object
`enrich`	a data frame of enrichment result.
`n`	number of points.
`delta`	the threshold of P value.

Value

scatter graph

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
sample2 <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
drawPointGraph(EnrichResult = sample2, n = 10, delta = 0.05)
```

`EnrichResult-class` *Class 'EnrichResult' This class represents the result of enrich analysis*

Description

Class 'EnrichResult' This class represents the result of enrich analysis

Slots

`enrich` a data frame of enrichment result

`test` Statistical test

`method` Multiple test correction methods

`m` the maximum number of ancestor layers for ontology enrichment

`maxGsize` The maximum number of DOTerm genes in enrichment analysis

`minGsize` The minimum number of DOTerm genes in enrichment analysis `traditional` Indicates whether the traditional ORA method is used

`delta` The highest p-value of significance for each node

`penalize` Whether to use penalty function in enrichment analysis

`interestGenes` A valid interest gene set

Author(s)

Haixiu Yang

`show,EnrichResult-method` *show method*

Description

show method for `EnrichResult` instance

Usage

```
## S4 method for signature 'EnrichResult'
show(object)
```

Arguments

`object`	A `EnrichResult` instance.

Value

print info

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102)
res <- doEnrich(interestGenes = demo.data, traditional = TRUE)
show(res)
```

`showDoTerms` *showDoTerms*

Description

show DOterms

Usage

```
showDoTerms(doterms = doterms)
```

Arguments

`doterms`	a data frame of DOterms.

Value

text

Author(s)

Haixiu Yang

Examples

```
mock_doterms <- data.frame(
  DOID = c("DOID:0000001", "DOID:0000002"),
  DOTerm = c("disease 1", "disease 2")
)
showDoTerms(mock_doterms)
```

`TermStruct` *Enrich_internal*

Description

Internal calculation of enrichment analysis

Usage

```
TermStruct(resultDO)
```

Arguments

`resultDO`	Receives the file output by the wrireResult function, which is used to visually display the enrichment results (without running the enrichment operation again).

Value

A `EnrichResult` instance.

Author(s)

Haixiu Yang

`viewDetailResult` *viewDetailResult method*

Description

viewDetailResult method for `EnrichResult` instance

Usage

```
viewDetailResult(object, ...)

## S4 method for signature 'EnrichResult'
viewDetailResult(object)
```

Arguments

`object`	A `EnrichResult` instance.
`...`	Additional arguments.

Value

data.frame of complete enrichment results

Author(s)

Haixiu Yang

Examples

```
# Assuming 'weighted_demo_result' is an EnrichResult object generated by doEnrich()
demo.data <- c(1636, 351, 102, 2932, 3077)
weighted_demo_result <- doEnrich(interestGenes=demo.data,
                         test="fisherTest",
                         method="holm",
                         m=1,
                         minGsize=10,
                         maxGsize=2000,
                         delta=0.05,
                         penalize=TRUE)
detail_df <- viewDetailResult(weighted_demo_result)
head(detail_df)
```

`viewSummaryResult` *viewSummaryResult method*

Description

viewSummaryResult method for `EnrichResult` instance

Usage

```
viewSummaryResult(object, P = 1, Q = 1, ...)

## S4 method for signature 'EnrichResult'
viewSummaryResult(object, P = 1, Q = 1)
```

Arguments

`object`	A `EnrichResult` instance.
`P`	pvalue cutoff.
`Q`	p.adjust cutoff.
`...`	Additional arguments.

Value

data.frame of standardized enrichment results

Author(s)

Haixiu Yang

Examples

```
# Assuming 'weighted_demo_result' is an EnrichResult object generated by doEnrich()
demo.data <- c(1636, 351, 102, 2932, 3077)
weighted_demo_result <- doEnrich(interestGenes=demo.data,
                        test="fisherTest",
                        method="holm",
                        m=1,
                        minGsize=10,
                        maxGsize=2000,
                        delta=0.05,
                        penalize=TRUE)
summary_df <- viewSummaryResult(weighted_demo_result)
head(summary_df)
```

`writeResult` *writeResult*

Description

Output enrichment result as text

Usage

```
writeResult(EnrichResult = NULL, file, Q = 1, P = 1)
```

Arguments

`EnrichResult`	the EnrichResult object
`file`	the address and name of the output file.
`Q`	Output only doterm information with p.adjust values less than or equal to Q.
`P`	Output only doterm information with p values less than or equal to P.

Value

text

Author(s)

Haixiu Yang

Examples

```
demo.data <- c(1636, 351, 102, 2932, 3077, 348, 4137, 54209)
sample4 <- doEnrich(interestGenes = demo.data, maxGsize = 100, minGsize = 10)
writeResult(EnrichResult = sample4, file = file.path(tempdir(), "result.txt"))
```

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