

Package ‘FoldGO’

March 30, 2021

Type Package

Title Package for Fold-specific GO Terms Recognition

Version 1.8.0

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Description FoldGO is a package designed to annotate gene sets derived from expression experiments and identify fold-change-specific GO terms.

Depends R (>= 4.0)

License GPL-3

Encoding UTF-8

LazyData true

biocViews DifferentialExpression, GeneExpression, GO, Software

RoxygenNote 6.1.0

Suggests knitr, rmarkdown, devtools, kableExtra

VignetteBuilder knitr

Imports topGO (>= 2.30.1), ggplot2 (>= 2.2.1), tidyr (>= 0.8.0), stats, methods

git_url <https://git.bioconductor.org/packages/FoldGO>

git_branch RELEASE_3_12

git_last_commit 79fa689

git_last_commit_date 2020-10-27

Date/Publication 2021-03-29

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examdata_bg	<i>Background sets of genes used in examples</i>
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Description

We used genes from two datasets in examples:

1. RNA-seq experiment on auxin treatment of Arabidopsis thaliana roots (degenes)
2. RNA-seq experiment on mRNA differential expression in LNCaP cells expressing the wild-type androgen receptor (AR-WT) or the ligand-independent AR-V7 splice variant (degenes_hum)

Usage

bggenes

bggenes_hum

Format

A vector containing the GeneIDs with 18039 and 38238 for A. thaliana and H. sapiens correspondingly

Source

1. A. thaliana and auxin: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE97258>
2. H. sapiens LNCap AR-V7: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE71334>

Examples

```
# load background genes from A. thaliana RNA-seq experiment
data("bggenes")
```

examdata_degs	<i>Differential expressed genes used in examples</i>
---------------	--

Description

We used two datasets in examples:

1. RNA-seq experiment on auxin treatment of Arabidopsis thaliana roots (degenes)
2. RNA-seq experiment on mRNA differential expression in LNCaP cells expressing the wild-type androgen receptor (AR-WT) or the ligand-independent AR-V7 splice variant (degenes_hum)

Usage

degenes
 degenes_hum

Format

A dataframes with 4 variables and 789 and 2079 for *A. thaliana* and *H. sapiens* correspondingly, where colnames are:

GeneID Gene identifier
FC fold-change value
pval p-value
qval Benjamini-Yekutieli adjusted p-value

Source

1. *A. thaliana* and auxin: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE97258>
2. *H. sapiens* LNCap AR-V7: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE71334>

Examples

```
# load degenes from RNA-seq experiment on auxin treatment of Arabidopsis thaliana roots
data("degenes")
```

examdata_objs	<i>Precompiled objects of GeneGroups, FuncAnnotGroups classes used in examples</i>
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Description

up_groups object of GeneGroups class compiled from up-regulated genes from rna-seq experiment on auxin treatment of *Arabidopsis thaliana* roots

down_groups object of GeneGroups class compiled from down-regulated genes from rna-seq experiment on auxin treatment of *Arabidopsis thaliana* roots

up_annotobj object of FuncAnnotGroups class compiled from lists of up-regulated genes from rna-seq experiment on auxin treatment of *Arabidopsis thaliana* roots

down_annotobj object of FuncAnnotGroups class compiled from lists of down-regulated genes from rna-seq experiment on auxin treatment of *Arabidopsis thaliana* roots

Usage

up_groups
 down_groups
 up_annotobj
 down_annotobj

Format

up_groups object of GeneGroups class
down_groups object of GeneGroups class
up_annotobj object of FuncAnnotGroupsTopGO class
up_annotobj object of FuncAnnotGroupsTopGO class

Examples

```
# load GeneGroups object with up-regulated genes from rna-seq experiment on auxin treatment
# of Arabidopsis thaliana roots
data("up_groups")
# load FuncAnnotGroups object compiled from lists of up-regulated genes
# from rna-seq experiment on auxin treatment of Arabidopsis thaliana roots
data("up_annotobj")
```

fagroupstopgo_class *S4 class for FuncAnnotGroupsTopGO object*

Description

This function conducts functional enrichment analysis for sets of genes generated by [GeneGroups](#) function.

Constructor

FuncAnnotGroupsTopGO(groups, namespace, customAnnot, annot, bggenes, ...), where:

groups - object of [GeneGroups](#) class

namespace - character string specifying GO namespace ("BP", "MF" or "CC")

customAnnot - Use if mapping argument is set to "custom". It can be an object generated by [GAFReader](#) or readGAF function from mgsa package or list which has GO term ids as keys and character vectors contain gene ids as values.

annot - from TopGO manual: These functions are used to compile a list of GO terms such that each element in the list is a character vector containing all the gene identifiers that are mapped to the respective GO term.

bggenes - vector contains background set of genes

... - other parameters:

genesannot - minimal number of genes annotated to a term in the annotation. 1 by default

algorithm - from TopGO manual: character string specifying which algorithm to use. The algorithms are shown by the topGO whichAlgorithms() function. "classic" by default

statistic - from TopGO manual: character string specifying which test to use. The statistical tests are shown by the topGO whichTests() function. "fisher" by default

mapping - from TopGO manual: character string specifying the name of the Bioconductor package containing the gene mappings for a specific organism. For example: mapping = "org.Hs.eg.db". "custom" by default

ID - from TopGO manual: character string specifying the gene identifier to use. Currently only the following identifiers can be used: c("entrez", "genbank", "alias", "ensembl", "symbol", "genename", "unigene")

Accessors

In the code examples below object is an object of FuncAnnotGroupsTopGO class

`getResultList(object)` - returns list of functional annotation result tables

Examples

```
# read .gaf file (in this example gaf file with annotation for A.thaliana is used)
library(topGO)
gaf_path <- system.file("extdata", "gene_association.tair.lzma",
                        package = "FoldGO", mustWork = TRUE)
# read gaf file and convert annotation in the list format
# contains GO term id's as keys and Gene ID's as values
gaf <- GAFReader(file = gaf_path, geneid_col = 10)
# split DEG genes into quantiles
gene_groups <- GeneGroups(degenes, 2)
# run enrichment test
annotobj <- FuncAnnotGroupsTopGO(gene_groups,"BP", customAnnot = gaf,
                                annot = topGO::annFUN.GO2genes,
                                bggenes = bggenes, padjmethod = "BH",
                                qitborder = 10, genesannot = 1)

# get results of functional enrichment analysis in a tabular form:
getResultList(annotobj)
```

foldspectest_class *FoldSpecTest S4 class*

Description

FoldSpecTest object calculates test on fold-specificity and stores all resulting data needed for further analysis. It takes object which is instance of subclass of AnnotGroups class (e.g. FuncAnnotGroupsTopGO class) as a minimal set of input parameters. For more details see Constructor section.

Constructor

`FoldSpecTest(annotgroups, fdrstep1, fdrstep2, padjmethod, fisher_alternative)`, where:

`annotgroups` - object of FuncAnnotGroups class

`fdrstep1` - FDR threshold for 1 step of fold-specificity recognition procedure

`fdrstep2` - FDR threshold for 2 step of fold-specificity recognition procedure

`padjmethod` - method for multiple testing correction (to see all possible methods print: `p.adjust.methods`)
Benjamini-Hochberg by default

`fisher_alternative` - indicates the alternative hypothesis and must be one of "two.sided", "greater" or "less". You can specify just the initial letter. Only used in the 2 by 2 case.

Accessors

In the code examples below object is an object of FoldSpecTest class

```
getFStable(object) - returns dataframe with fold-change-specific terms and related data
getNFStable(object) - returns dataframe with not fold-change-specific terms and related data
getResultTable(object) - returns dataframe with both fold-change-specific and not fold-change-specific terms
getWholeIntName(object) - returns name of largest fold-change interval (DEGs interval)
```

Examples

```
# FoldSpecTest function requires only object of FuncAnnotGroups class as a
# minimal set of parameters. In the example up_annotobj is an object of FuncAnnotGroups class
# compiled from lists of up-regulated genes from rna-seq experiment on auxin treatment
# of Arabidopsis thaliana roots [FoldGO::up_annotobj].
FoldSpecTest(up_annotobj)

# FoldSpecTest function with custom parameters
fs_up <- FoldSpecTest(up_annotobj, fdrstep1 = 0.2, fdrstep2 = 0.01, padjmethod = "BY")

# get dataframe with fold-change-specific terms
getFStable(fs_up)

# get dataframe with not fold-change-specific terms
getNFStable(fs_up)

# get dataframe with both fold-change-specific and not fold-change-specific terms
getResultTable(fs_up)

# get name of largest fold-change interval (DEGs interval)
getWholeIntName(fs_up)
```

gafreader_class

S4 class for GAFReader object

Description

Parser for annotation presented in GAF file format (.gaf). GAFReader function returns object which contains as a dataframe annotation as it presented in initial file. Via GAFReader accessor method one can retrieve annotations as list GO term id's as keys and Gene ID's as values and version of file (see Accessors section).

Constructor

GAFReader(file = gaf_path, geneid_col = 10), where:

file - full path to annotation file

geneid_col - index of column with Gene ID (2 by default)

Accessors

In the code examples below object is an object of GAFReader class

getVersion(object) - returns version of GAF file

getAnnotation(object) - returns annotation from GAF file in form of GO ids - Gene ids list

Methods

In the code examples below object is an object of GAFReader class

getAnnotation(object) - Convert annotation to list contains GO term id's as keys and Gene ID's as values

Examples

```
# read .gaf file (in this example gaf file with annotation for A.thaliana is used)
# object returned by \link{GAFReader} can be used by
# \link{FuncAnnotGroupsTopGO} function.
gaf_path <- system.file("extdata", "gene_association.tair.lzma",
                        package = "FoldGO", mustWork = TRUE)
gaf <- GAFReader(file = gaf_path, geneid_col = 10)
# get version of file
getVersion(gaf)
# get annotation in the list format contains GO term id's as keys and Gene ID's as values
getAnnotation(gaf)
```

genegroups_class

S4 class for Gene Groups

Description

This function splits gene list into quantiles and generates all unions of neighbouring quantiles. It takes dataframe with genes ID's and fold values, number of quantiles and logical variable which must set to TRUE if fold values are presented in logarithmic scale, otherwise it must be set to FALSE value (TRUE by default) as parameters.

Constructor

GeneGroups(inputtable, quannumber, logfold), where:

inputtable - dataframe contains initial set of genes gene ID's in the first row and corresponding fold change values in the second row

quannumber - number of quantiles (e.g. 2,3,4...)

logfold - TRUE if fold values are presented in log scale, otherwise is FALSE

Accessors

In the code examples below object is an object of GeneGroups class

```
getGroups(object) - returns list of gene sets for each quartile and all combinations
getWholeIntName(object) - returns name of the interval containing all differentially expressed
genes
getQuanNumber(object) - returns number of quantiles
getIntNames(object) - returns vector of intervals names
getRegType(object) - returns regulation type
```

Examples

```
# split initial gene set into quantiles
gene_groups <- GeneGroups(degenes, 6)
# get list of gene sets for each quartile and all combinations
getGroups(gene_groups)
# get name of the interval containing all differentially expressed genes
getWholeIntName(gene_groups)
# get number of quantiles
getQuanNumber(gene_groups)
# get vector of intervals names
getIntNames(gene_groups)
# get regulation type
getRegType(gene_groups)
```

getAnnotation

Get annotation derived from annotation file

Description

This method allows to retrieve annotation from MgsaSets or [GAFReader](#) class object in form of list contains GO term id's as keys and Gene ID's as values

Usage

```
getAnnotation(object)

## S4 method for signature 'AnnotationReader'
getAnnotation(object)

## S4 method for signature 'list'
getAnnotation(object)

## S4 method for signature 'MgsaSets'
getAnnotation(object)

## S4 method for signature '`NULL`'
getAnnotation(object)
```

Arguments

object - Object of mgsa package MgsaSets class or FoldGO [GAFReader](#) class

Value

list contains GO term id's as keys and Gene ID's as values

Examples

```
## Not run:
gaf_path <- system.file("extdata", "gene_association.tair.lzma",
                        package = "FoldGO", mustWork = TRUE)
gaf <- GAFReader(file = gaf_path, geneid_col = 10)
getAnnotation(gaf)

## End(Not run)
```

getWholeIntName *getWholeIntName S4 method*

Description

This method returns name of the interval containing all differentially expressed genes. It can be applied to objects of GeneGroups and FoldSpecTest classes

Arguments

object Object of GeneGroups or FoldSpecTest class

See Also

[FoldSpecTest GeneGroups](#)

Examples

```
# GeneGroups class object example
gene_groups <- GeneGroups(degenes, 6)
getWholeIntName(gene_groups)
# FoldSpecTest class object example
fs_up <- FoldSpecTest(up_annotobj)
getWholeIntName(fs_up)
```

plot, FoldSpecTest, ANY-method
Fold-change specific GO Profile chart plotting

Description

Fold-change specific GO Profile chart plotting

Usage

```
## S4 method for signature 'FoldSpecTest,ANY'
plot(x, y, x_text_size = 10)
```

Arguments

`x` - object of S4 FoldSpecTest class with up-regulated genes
`y` - object of S4 FoldSpecTest class with down-regulated genes
`x_text_size` - x axis labels size

Value

- Fold-change specific GO Profile plot

Examples

```
# calculate fold-specificity test for up-regulated genes
up_fs <- FoldSpecTest(up_annotobj)
# calculate fold-specificity test for down-regulated genes
down_fs <- FoldSpecTest(down_annotobj)
plot(up_fs, down_fs)
```

rna_seq_data	<i>Data from rna-seq experiment on auxin treatment of Arabidopsis thaliana roots</i>
--------------	--

Description

A dataset containing the GeneIDs and corresponding fold-change values.

Usage

```
rna_seq_data
```

Format

A data frame with 18039 rows and 4 variables:

GeneID Gene identifier

FC fold-change value

pval p-value

qval Benjamini-Yekutieli adjusted p-value

Source

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE97258>

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