Package ‘rSEA’

October 14, 2022

Type Package

Title Simultaneous Enrichment Analysis

Version 2.1.1

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Description

SEA performs simultaneous feature-set testing for (gen)omics data. It tests the unified null hypothesis controls the family-wise error rate for all possible pathways. The unified null hypothesis is defined as: "The proportion of true features in the set is less than or equal to the threshold c", where c is selected by the user. Family-wise error rate control is provided through use of closed testing with Simes test. For more information on closed testing with Simes see Goeman et al. (2019) <doi:10.1093/biomet/asz041> and for more information about the properties and performance of SEA procedure see Ebrahimpoor et al. (2019) <doi:10.1093/bib/bbz074>.

URL https://github.com/mitra-ep/rSEA

Depends R (>= 2.10), hommel (>= 1.4), ggplot2

Suggests knitr, rmarkdown

License GPL (>= 2)

Date 2020-03-23

Encoding UTF-8

VignetteBuilder knitr

LazyData true

RoxygenNote 6.1.1

NeedsCompilation no

Repository CRAN

Date/Publication 2020-03-23 11:30:02 UTC
Description

This package uses raw p-values of genomic features as input and evaluates any given list of feature-sets or pathways. For each set the adjusted p-value and TDP lower-bound are calculated. The type of test can be defined by arguments and can be refined as necessary. The p-values are corrected for every possible set of features, making the method flexible in choice of pathway list and test type. For more details see: Ebrahimpoor, M (2019) <doi:10.1093/bib/bbz074>

Details

The unified null hypothesis is tested using closed testing procedure and all-resolutions inference. It combines the self-contained and competitive approaches in one framework. In short, using p-values of the individual features as input, the package can provide an FWER-adjusted p-value along with a lower bound and a point estimate for the proportion of true discoveries per feature-set. The flexibility in revising the choice of feature-sets without inflating type-I error is the most important property of SEA.

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References

Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods, Briefings in Bioinformatics,bbz074 https://doi.org/10.1093/bib/bbz074
plotSEA

Description
returns a plot of SEA-chart which illustrates proportion of discoveries per pathway.

Usage
plotSEA(object, by = "TDP.estimate", threshold = 0.005, n = 20)

Arguments
object A SEA-chart object which is the output of SEA function
by the Variable which will we mapped. It should be either the TDP estimate or TDP bound. The default is TDP bound.
threshold A real number between 0 and 1. Which will be used as a visual aid to distinguish significant pathways
n Integer. Number of rows from SEA-chart object to be plotted.

Value
Returns a plot of SEA_chart according to the selected arguments

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References
Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods, Briefings in Bioinformatics, bbz074

See Also
SEA

Examples
#See the examples for \code{\link{SEA}}
Description

returns SEA chart (a data.frame) including the test results and estimates for the specified feature-sets from pathlist.

Usage

SEA(pvalue, featureIDs, data, pathlist, select, tdphat = TRUE, selfcontained = TRUE, competitive = TRUE, thresh = NULL, alpha = 0.05)

Arguments

pvalue Vector of p-values. It can be the name of the covariate representing the Vector of all raw p-values in the data or a single vector but in the latter case it should match the featureIDs vector

featureIDs Vector of feature IDs. It can be the name of the covariate representing the IDs in the data or a single vector but in the latter case it should match the pvalue vector

data Optional data frame or matrix containing the variables in pvalue and featureIDs

pathlist A list containing pathways defined by featureIDs. Checkout the vignette for more details and available codes to create your own pathway

select A vector. Number or names of pathways of interest from the pathlist of choice. If missing, all pathways of the database will be included

tdphat Logical. If TRUE the point estimate of the True Discoveries Proportion within each pathway will be calculated

selfcontained Logical. If TRUE the self-contained null hypothesis will be tested for each pathway and the corresponding adj. p-value is returned

competitive Logical. If TRUE the default competitive null hypothesis will be tested for each pathway and the corresponding adj. p-value is returned, you can define a threshold with thresh argument

thresh A real number between 0 and 1. If specified, the competitive null hypothesis will be tested against this threshold for each pathway and the corresponding adj. p-value is returned

alpha The type I error allowed for TDP bound. The default is 0.05.

Value

A data.frame is returned including a list of pathways with corresponding TDP bound estimate, and if specified, TDP point estimate and adjusted p-values
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References

Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods, Briefings in Bioinformatics, , bbz074, https://doi.org/10.1093/bib/bbz074

See Also

setTest, topSEA,

Examples

## Not run:
##Generate a vector of pvalues for a toy example
set.seed(159)

m<- 100
pvalues <- runif(m,0,1)^5
featureIDs <- as.character(1:m)

# perform a self-contained test for all features
setTest(pvalues, featureIDs, testype = "selfcontained")

# create 3 random pathway of size 60, 20 and 45
randpathlist=list(A=as.character(c(sample(1:m, 60))),
                 B=as.character(c(sample(1:m, 20)) ),
                 C=as.character(c(sample(1:m, 45))))

# get the seachart for the whole pathlist
S1<-SEA(pvalues, featureIDs, pathlist=randpathlist)
S1

# get the seachart for only first two pathways of the randpathlist
S2<-SEA(pvalues, featureIDs, pathlist=randpathlist, select=1:2)
S2

#sort the list by competitive p-value and select top 2
topSEA(S2, by=Comp.adjP, descending = FALSE, n=2)

#make an enrichment plot based on TDP.estimated of te pathways
#here pathways with more than 20% active signals will be identified
plotSEA(S1,threshold = 0.20,n=3)

## End(Not run)
Description

Estimates the TDP of the specified set of features.

Usage

\texttt{setTDP(pvalue, featureIDs, data, set, alpha = 0.05)}

Arguments

- **pvalue**: The vector of p-values. It can be the name of the covariate representing the Vector of raw p-values in the \texttt{data} or a single vector but in the latter case it should match the \texttt{featureIDs} vector.
- **featureIDs**: The vector of feature IDs. It can be the name of the covariate representing the IDs in the \texttt{data} or a single vector but in the latter case it should match the \texttt{pvalue} vector.
- **data**: Optional data frame or matrix containing the variables in \texttt{pvalue} and \texttt{featureIDs}.
- **set**: The selection of features defining the feature-set based on the the \texttt{featureIDs}. If missing, the set of all features is evaluated.
- **alpha**: The type I error allowed. The default is 0.05. NOTE: this should be consistent across the study.

Value

A named vector including the lower bound and point estimate for the true discovery proportion (TDP) of the specified test for the feature-set is returned.

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References

Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods, Briefings in Bioinformatics, , bbz074, https://doi.org/10.1093/bib/bbz074

See Also

\texttt{setTest, SEA}
Examples

```r
## Not run:
set.seed(159)
# generate random p-values with pseudo IDs
m<- 100
pvalues <- runif(m,0,1)^5
featureIDs <- as.character(1:m)

# perform a self-contained test for all features
settest(pvalues, featureIDs, testype = "selfcontained")

# estimate the proportion of true discoveries among all m features
settdp(pvalues, featureIDs)

# create a random pathway of size 60
randset=as.character(c(sample(1:m, 60)))

# estimate the proportion of true discoveries in a random set of size 50
settdp(pvalues, featureIDs, set=randset)

## End(Not run)
```

Description

calculates the adjusted p-value for the local hypothesis as defined by testtype and testvalue.

Usage

```r
setTest(pvalue, featureIDs, data, set, testype, testvalue)
```

Arguments

- **pvalue**: The vector of p-values. It can be the name of the covariate representing the vector of raw p-values in the data or a single vector but in the latter case it should match the featureIDs vector.
- **featureIDs**: The vector of feature IDs. It can be the name of the covariate representing the IDs in the data or a single vector but in the latter case it should match the pvalue vector.
- **data**: Optional data frame or matrix containing the variables in pvalue and featureIDs.
- **set**: The selection of features defining the feature-set based on the featureIDs. If missing, the set of all features is selected.
testype  Character, type of the test: "selfcontained" or "competitive". Choosing the self-
    contained option will automatically set the threshold to zero and the testvalue
    is ignored. Choosing the competitive option without a testvalue will set the
    threshold to the overall estimated proportion of true hypotheses.

testvalue  Optional value to test against. Setting this value to c along with testype="competitive"
    will lead to testing the null hypothesis against a threshold c. Note: this value
    needs to be a proportion.

Value

The adjusted p-value of the specified test for the feature-set is returned.

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References

Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous
Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods,
Briefings in Bioinformatics, , bbz074, https://doi.org/10.1093/bib/bbz074

See Also

setTDP SEA

Examples

```r
## Not run:
#Generate a vector of pvalues
set.seed(159)

m<- 100
pvalues <- runif(m,0,1)^5
featureIDs <- as.character(1:m)

# perform a self-contained test for all features
settest(pvalues, featureIDs, testype = "selfcontained")

# create a random pathway of size 60
randset=as.character(c(sample(1:m, 60)))

# perform a competitive test for the random pathway
settest(pvalues, featureIDs, set=randset, testype = "competitive")

# perform a unified null hypothesis test against 0.2 for a set of size 50
settest(pvalues, featureIDs, set=randset, testype = "competitive", testvalue = 0.2 )
```
## Description

returns a permutation of SEA-chart which rearranges the feature-sets according to the selected argument into ascending or descending order.

## Usage

topSEA(object, by, thresh = NULL, descending = TRUE, n = 20, cover)

## Arguments

- **object**: A SEA-chart object which is the output of `SEA` function.
- **by**: Variable name by which the ordering should happen. It should be a column of SEA-chart. The default is TDP_bound.
- **thresh**: A real number between 0 and 1. If specified the values of the variable defined in by will be thresholded accordingly.
- **descending**: Logical. If TRUE The output chart is organized in a descending order.
- **n**: Integer. Number of rows of the output chart.
- **cover**: An optional threshold for coverage, which must be a real number between 0 and 1. If specified, feature-sets with a coverage lower than or equal to this value are removed.

## Value

Returns a subset of SEA_chart sorted according to the arguments.

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## References

Mitra Ebrahimpoor, Pietro Spitali, Kristina Hettne, Roula Tsonaka, Jelle Goeman, Simultaneous Enrichment Analysis of all Possible Gene-sets: Unifying Self-Contained and Competitive Methods, Briefings in Bioinformatics, bbz074

## See Also

`SEA`
Examples

#See the examples for \code{\link{SEA}}
Index

* rSEA
  rSEA-package, 2

plotSEA, 3
rSEA-package, 2

SEA, 3, 4, 6, 8, 9
setTDP, 6, 8
setTest, 5, 6, 7

topSEA, 5, 9