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R topics documented:

fdrci-package	2
FDRplot	3
fdrTbl	4
fdr_od	7
MV_q	9

Index	12
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fdrci-package

Permutation-Based FDR Point and Confidence Interval Estimation

Description

FDR functions for permutation-based estimators, including π_0 as well as FDR confidence intervals. The confidence intervals account for dependencies between tests by the incorporation of an overdispersion parameter, which is estimated from the permuted data.

Details

Package: fdrci
Type: Package
Version: 2.1
Date: 2018-02-21
License: Artistic-2.0
LazyLoad: yes

This method is designed to compute FDR when a permutation-based approach has been utilized. The objective here is to identify a subset of positive tests that have corresponding statistics with a more extreme distribution than the permuted results, which are assumed to represent the null. The significance of the subset is described in terms of the FDR and uncertainty in the FDR estimate by computing a confidence interval. Say a set of p-values (or simply a set of test statistics) were recorded for a set of hypothesis tests, and data were permuted B times with test results generated for each permutation. The function `fdr_od()` can be used to estimate FDR and a confidence interval along with π_0 , the proportion of true null hypotheses, given a selected significance threshold. The function `fdrTbl()` uses `fdr_od()` to create a table of results over a sequence of possible significance thresholds. Finally, the function `FDRplot` will plot results from `fdrTbl()`, facilitating the selection of a final significance threshold.

Author(s)

Joshua Millstein

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References

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

`FDRplot`*Plot results of FDR table generated by `fdrTbl()`*

Description

This function plots FDR point and CI estimates over a sequence of possible significance thresholds. Results from `fdrTbl()` can be plotted directly as input to `FDRplot`.

Usage

```
FDRplot(  
  plotdat,  
  lowerbound,  
  upperbound,  
  ymax = 1,  
  annot = "",  
  xpos = 0.8,  
  ypos = 0.8  
)
```

Arguments

<code>plotdat</code>	a table that is returned from <code>fdrTbl()</code> , or results formatted in the same way.
<code>lowerbound</code>	$-\log_{10}(\text{p-value})$ lower bound for the x-axis of the plot.
<code>upperbound</code>	$-\log_{10}(\text{p-value})$ upper bound for the x-axis of the plot.
<code>ymax</code>	upper limit for range of the y-axis.
<code>annot</code>	annotation text to be added to plot area.
<code>xpos</code>	x-axis position for <code>annot</code>
<code>ypos</code>	y-axis position for <code>annot</code>

Value

ggplot2 object

Author(s)

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Joshua Millstein

References

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

Examples

```

ss = 100
nvar = 100
X = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
e = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
Y = .1*X + e
nperm = 10

myanalysis = function(X,Y){
  ntests = ncol(X)
  rslts = as.data.frame(matrix(NA,nrow=ntests,ncol=2))
  names(rslts) = c("ID","pvalue")
  rslts[,"ID"] = 1:ntests
  for(i in 1:ntests){
    fit = cor.test(X[,i],Y[,i],na.action="na.exclude",
                  alternative="two.sided",method="pearson")
    rslts[i,"pvalue"] = fit$p.value
  }
  return(rslts)
} # End myanalysis

# Generate observed results
obs = myanalysis(X,Y)

# Generate permuted results
perml = vector('list',nperm)
for(perm in 1:nperm){
  X1 = X[order(runif(nvar)),]
  perml[[perm]] = myanalysis(X1,Y)
}

# FDR results table
myfdrtbl = fdrTbl(obs$pvalue,perml,"pvalue",nvar,0,3)
# Plot results
FDRplot(myfdrtbl,0,3,annot="A. An Example")

```

fdrTbl

FDR Estimate and Confidence Interval Sequence Table

Description

Computes FDR estimates and confidence intervals for a sequence of potential significance thresholds.

Usage

```

fdrTbl(
  obs.vec,

```

```

perm.list,
pname,
ntests,
lowerbound,
upperbound,
incr = 0.1,
cl = 0.95,
c1 = NA,
correct = "none"
)

```

Arguments

obs.vec	observed vector of p-values.
perm.list	list of dataframes that include a column of permutation p-values (or statistics) in each. The length of the list perm = number of permutations.
pname	name of column in each list component dataframe that includes p-values (or statistics).
ntests	total number of observed tests, which is usually the same as the length of obs.vec and the number of rows in each perm.list dataframe. However, this may not be the case if results were filtered by a p-value threshold or statistic threshold. If filtering was conducted then lowerbound must be greater (more extreme) than the filtering criterion.
lowerbound	lowerbound refers to the range of $-\log_{10}(\text{p-value})$ over which fdr is computed for a sequence of thresholds
upperbound	upperbound refers to the range of $-\log_{10}(\text{p-value})$ over which fdr is computed for a sequence of thresholds
incr	value by which to increment the sequence from lowerbound to upperbound on a $-\log_{10}(\text{p-value})$ scale. Default is 0.1.
cl	confidence level (default is .95).
c1	overdispersion parameter to account for dependencies among tests. If all tests are known to be independent, then this parameter should be set to 1.
correct	"none", "BH", should confidence intervals be corrected for multiplicity using a modification of the Benjamini and Yekutieli (2005) approach for selecting and correcting intervals? (default is "none")

Details

fdrTbl calls fdr_od for a series of discovery thresholds. Output from fdrTbl() can be used for FDRplot() input.

If correct = "BH", then confidence intervals will be corrected according to the thresholds specified by lowerbound, upperbound, and incr. Thresholds will be selected if FDR is determined to be significantly different than 1. First a Z-score test is conducted using the Millstein & Volfson standard error estimate. Then BH FDR is computed according to the Benjamini and Yekutieli (2005) approach. CIs for selected thresholds will be adjusted to account for multiple CI estimation. For thresholds that are not selected, NA values are returned.

Value

A dataframe is returned where rows correspond to p-value thresholds in the sequence from lower-bound to upperbound and columns are: c("threshold", "fdr", "l1", "ul", "pi0", "odp", "S", "Sp")

threshold	p-value threshold chosen to define positive tests
fdr	estimated FDR at the chosen p-value threshold
l1	estimated lower 95% confidence bound for the FDR estimate
ul	estimated upper 95% confidence bound for the FDR estimate
pi0	estimated percent of true null hypotheses
odp	estimated over-dispersion parameter
S	observed number of positive tests
Sp	total number of positive tests summed across all permuted result sets

Author(s)

Joshua Millstein

References

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

Benjamini, Yoav, and Daniel Yekutieli. "False discovery rate adjusted multiple confidence intervals for selected parameters." *Journal of the American Statistical Association* 100.469 (2005): 71-81.

Examples

```
n.row=100
n.col=100
X = as.data.frame(matrix(rnorm(n.row*n.col),nrow=n.row,ncol=n.col))
e = as.data.frame(matrix(rnorm(n.row*n.col),nrow=n.row,ncol=n.col))
Y = .1*X + e
nperm = 10

myanalysis = function(X,Y){
  ntests = ncol(X)
  rslts = as.data.frame(matrix(NA,nrow=ntests,ncol=2))
  names(rslts) = c("ID","pvalue")
  rslts[,"ID"] = 1:ntests
  for(i in 1:ntests){
    fit = cor.test(X[,i],Y[,i],na.action="na.exclude",
    alternative="two.sided",method="pearson")
    rslts[i,"pvalue"] = fit$p.value
  }
  return(rslts)
} # End myanalysis
```

```

## Generate observed results
obs = myanalysis(X,Y)

## Generate permuted results
perml = vector('list',nperm)
for(perm in 1:nperm){
  X1 = X[order(runif(n.col)),]
  perml[[perm]] = myanalysis(X1,Y)
}

## FDR results table
fdrTbl(obs$pvalue,perml,"pvalue",n.col,1,2)
fdrTbl(obs$pvalue,perml,"pvalue",n.col,1,2,correct="BH")

```

fdr_od

*Permutation-Based FDR and Confidence Interval***Description**

This function can be used to estimate FDR, corresponding confidence interval, and π_0 , the proportion of true null hypotheses, given a selected significance threshold, and results from permuted data.

Usage

```
fdr_od(obsp, permp, pnm, ntests, thres, cl = 0.95, c1 = NA)
```

Arguments

obsp	observed vector of p-values.
permp	list of dataframes that include a column of permutation p-values (or statistics) in each. The length of the list permp = number of permutations.
pnm	name of column in each list component dataframe that includes p-values (or statistics).
ntests	total number of observed tests, which is usually the same as the length of obsp and the number of rows in each permp dataframe. However, this may not be the case if results were filtered by a p-value threshold or statistic threshold. If filtering was conducted then thres must be smaller (more extreme) than the filtering criterion.
thres	significance threshold.
cl	confidence level (default is .95).
c1	overdispersion parameter. If this parameter is not specified (default initial value is NA), then the parameter is estimated from the data. If all tests are known to be independent, then this parameter should be set to 1.

Details

If a very large number of tests are conducted, it may be useful to filter results, that is, save only results of those tests that meet some relaxed nominal significance threshold. This alleviates the need to record results for tests that are clearly non-significant. Results from `fdr_od()` are valid as long as `thres <` the relaxed nominal significance threshold for both observed and permuted results. It is not necessary for the input to `fdr_od()` to be p-values, however, `fdr_od()` is designed for statistics in which smaller values are more extreme than larger values as is the case for p-values. Therefore, if raw statistics are used, then a transformation may be necessary to insure that smaller values are more likely associated with false null hypotheses than larger values. In certain situations, for instance when a large proportion of tests meet the significance threshold, π_0 is estimated to be very small, and thus has a large influence on the FDR estimate. To limit this influence, π_0 is constrained to be .5 or greater, resulting in a more conservative estimate under these conditions.

Value

A list which includes:

FDR	FDR point estimate
ll	lower confidence limit
ul	upper confidence limit
π_0	proportion of true null hypotheses
c1	overdispersion parameter
S	observed number of positive tests
Sp	total number of positive tests summed across all permuted result sets

Author(s)

Joshua Millstein

References

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

Examples

```
ss=100
nvar=100
X = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
e = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
Y = .1*X + e
nperm = 10

myanalysis = function(X,Y){
  ntests = ncol(X)
  rslts = as.data.frame(matrix(NA,nrow=ntests,ncol=2))
  names(rslts) = c("ID","pvalue")
```



```

rslts[,"ID"] = 1:ntests
for(i in 1:ntests){
  fit = cor.test(X[,i],Y[,i],na.action="na.exclude",
  alternative="two.sided",method="pearson")
  rslts[i,"pvalue"] = fit$p.value
}
return(rslts)
} # End myanalysis

# Generate observed results
obs = myanalysis(X,Y)

## Generate permuted results
perml = vector('list',nperm)
for(p_ in 1:nperm){
  X1 = X[order(runif(nvar)),]
  perml[[p_]] = myanalysis(X1,Y)
}

## FDR results
fdr_od(obs$pvalue,perml,"pvalue",nvar,.05)

```

MV_q

MV q-values and confidence intervals

Description

q-values with confidence intervals are generated, based in the Millstein and Volfson (MV) estimators.

Usage

```
MV_q(obsp, permpp, pnm, ntests, cl = 0.95, c1 = NA)
```

Arguments

obsp	observed vector of p-values.
permpp	list of dataframes that include a column of permutation p-values (or statistics) in each. The length of the list permpp = number of permutations.
pnm	name of column in each list component dataframe that includes p-values (or statistics).
ntests	total number of observed tests, which is usually the same as the length of obsp and the number of rows in each permpp dataframe. However, this may not be the case if results were filtered by a p-value threshold or statistic threshold. If filtering was conducted then thres must be smaller (more extreme) than the filtering criterion.
cl	confidence level (default is .95).

c1 overdispersion parameter. If this parameter is not specified (default initial value is NA), then the parameter is estimated from the data. If all tests are known to be independent, then this parameter should be set to 1.

Details

Millstein and Volfson (2013) FDR is based on the idea that FDR is estimated at a level specified by the investigator. Storey and Tibshirani (2003) developed the q-value concept, where FDR is estimated at each observed p-value. However, Millstein and Volfson argued that in order to be informative, uncertainty in the estimate should be quantified, thus the development of confidence intervals for FDR. The MV FDR estimator is less conservative than the BH estimator.

Value

A dataframe which includes:

q	q-value corresponding to the respective p-value
q.l1	q-value lower limit
q.u1	q-value upper limit

Author(s)

Joshua Millstein

References

Millstein J, Volfson D. 2013. Computationally efficient permutation-based confidence interval estimation for tail-area FDR. *Frontiers in Genetics | Statistical Genetics and Methodology* 4(179):1-11.

Storey, John D., and Robert Tibshirani. "Statistical significance for genomewide studies." *Proceedings of the National Academy of Sciences* 100.16 (2003): 9440-9445.

Examples

```
ss=100
nvar=100
X = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
e = as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))
Y = .1*X + e
nperm = 10

myanalysis = function(X,Y){
  ntests = ncol(X)
  rslts = as.data.frame(matrix(NA,nrow=ntests,ncol=2))
  names(rslts) = c("ID","pvalue")
  rslts[,"ID"] = 1:ntests
  for(i in 1:ntests){
    fit = cor.test(X[,i],Y[,i],na.action="na.exclude",
    alternative="two.sided",method="pearson")
    rslts[i,"pvalue"] = fit$p.value
  }
  return(rslts)
}
```

```
} # End myanalysis

# Generate observed results
obs = myanalysis(X,Y)

# Generate permuted results
perml = vector('list',nperm)
for(p_ in 1:nperm){
  X1 = X[order(runif(nvar)),]
  perml[[p_]] = myanalysis(X1,Y)
}

q.values.MV = MV_q(obs$pvalue,perml,"pvalue",nvar)
```

Index

* **htest**

fdr_od, 7

fdrCi-package, 2

fdrTbl, 4

* **nonparametric**

fdr_od, 7

fdrCi-package, 2

fdrTbl, 4

fdr_od, 7

fdrCi (fdrCi-package), 2

fdrCi-package, 2

FDRplot, 3

fdrTbl, 4

MV_q, 9