Package ‘fdrci’

June 11, 2021

Type Package
Title Permutation-Based FDR Point and Confidence Interval Estimation
Version 2.2
Date 2021-6-9
Encoding UTF-8
Imports ggplot2, stats
Description FDR functions for permutation-based estimators, including pi0 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.
License Artistic-2.0
LazyLoad yes
RoxygenNote 7.1.1
NeedsCompilation no
Author Joshua Millstein [aut, cre]
Maintainer Joshua Millstein <joshua.millstein@usc.edu>
Repository CRAN
Date/Publication 2021-06-11 19:10:02 UTC

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Description

FDR functions for permutation-based estimators, including pi0 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 pi0, 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

Maintainer: Joshua Millstein <millsteinjoshua@gmail.com> Joshua Millstein

References

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

Arguments
- `plotdat`: a table that is returned from fdrTbl(), or results formatted in the same way.
- `lowerbound`: -log10(p-value) lower bound for the x-axis of the plot.
- `upperbound`: -log10(p-value) upper bound for the x-axis of the plot.
- `ymax`: upper limit for range of the y-axis.
- `annot`: annotation text to be added to plot area.
- `xpos`: x-axis position for annot
- `ypos`: y-axis position for annot

Value
- ggplot2 object

Author(s)
Joshua Millstein, <joshua.millstein@usc.edu>
Joshua Millstein

References

Examples

\[
\begin{align*}
ss &= 100 \\
nvar &= 100 \\
X &= \text{as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))} \\
e &= \text{as.data.frame(matrix(rnorm(ss*nvar),nrow=ss,ncol=nvar))} \\
Y &= 0.1 \times X + e \\
nperm &= 10
\end{align*}
\]

```
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(quotesingle.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,
  perml,
  pvalue,
  nvar,
  q,
  type,
  plot,
  annotate
)```

### fdrTbl

```r
perm.list,
pname,
ntests,
lowerbound,
upperbound,
icr = 0.1,
c1 = 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 permp = 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 -log10(p-value) over which fdr is computed for a sequence of thresholds.

- **upperbound**
  - upperbound refers to the range of -log10(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 -log10(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","ll","ul","pi0","odp","S","Sp")

threshold  p-value threshold chosen to define positive tests
fdr        estimated FDR at the chosen p-value threshold
ll         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


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 \(\pi_0\), 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, `pi0` is estimated to be very small, and thus has a large influence on the FDR estimate. To limit this influence, `pi0` 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
- `pi0`: 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


Examples

```r
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")
nrow=ntests,ncol=2))
  names(rslts) = c("ID","pvalue")

```
MV_q

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

Usage

MV_q(obsp, permp, pnm, ntests, 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.
c1 confidence level (default is .95).
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.ll  q-value lower limit
- q.ul  q-value upper limit

Author(s)

Joshua Millstein

References


Examples

```r
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=nperm,ncol=ntests))
  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)
}
```
MV_q

) # 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)
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