

Package ‘calm’

September 27, 2023

Type Package

Title Covariate Assisted Large-scale Multiple testing

Version 1.15.0

Description Statistical methods for multiple testing with covariate information. Traditional multiple testing methods only consider a list of test statistics, such as p-values. Our methods incorporate the auxiliary information, such as the lengths of gene coding regions or the minor allele frequencies of SNPs, to improve power.

License GPL (>=2)

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LazyData false

Imports mgcv, stats, graphics

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VignetteBuilder knitr

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calm

*Covariate Assisted Large-scale Multiple testing***Description**

Statistical methods for multiple testing with covariate information.

Details

Package: calm
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Author(s)

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References

Liang, K (2019) *Empirical Bayes analysis of RNA sequencing experiments with auxiliary information*.

See Also

[CLfdr](#)

CLfdr *Conditional local FDR (CLfdr)*

Description

CLfdr returns the local false discovery rate (FDR) conditional on auxiliary covariate information

Usage

```
CLfdr(x, y, pval = NULL, pi0.method = "RB", bw.init = NULL,
      bw = NULL, reltol = 1e-04, n.subsample = NULL, check.gam = FALSE,
      k.gam = NULL, info = TRUE)
```

Arguments

x	covariates, could be a vector of length m or a matrix with m rows.
y	a vector of z -values of length m .
pval	a vector of p -values of length m . The p -values are only used to compute the overall true null proportion when <code>pi0.method="RB"</code> .
pi0.method	method to estimate the overall true null proportion (π_0). "RB" for the right-boundary procedure (Liang and Nettleton, 2012, JRSSB) or "JC" (Jin and Cai, 2007, JASA).
bw.init	initial values for bandwidth, optional. If not specified, normal-reference rule will be used.
bw	bandwidth values.
reltol	relative tolerance in optim function.
n.subsample	size of the subsample when estimating bandwidth.
check.gam	indicator to perform <code>gam.check</code> function on the nonparametric fit.
k.gam	tuning parameter for <code>mgcv::gam</code> .
info	indicator to print out fitting information.

Details

In many multiple testing applications, the auxiliary information is widely available and can be useful. Such information can be summary statistics from a similar experiment or disease, the lengths of gene coding regions, and minor allele frequencies of SNPs.

y is a vector of m z -values, one of each hypothesis under test. The z -values follow $N(0,1)$ if their corresponding null hypotheses are true. Other types of test statistics, such as t -statistics and p -values can be transformed to z -values. In practice, if the distribution of z -values is far from $N(0,1)$, recentering and rescaling of the z -values may be necessary.

x contains auxiliary covariate information. For a single covariate, x should be a vector of length m . For multiple covariates, x should be a matrix with m rows. The covariates can be either continuous or ordered.

`pi0.method` specifies the method used to estimate the overall true null proportion. If the z -values are generated from the normal means model, the "JC" method from Jin and Cai (2007) JASA can be a good candidate. Otherwise, the right-boundary procedure ("RB", Liang and Nettleton, 2012, JRSSB) is used.

`bw` are bandwidth values for estimating local alternative density. Suppose there are p covariates, then `bw` should be a vector of $p+1$ positive numerical values. By default, these bandwidth values are chosen by cross-validation to minimize a certain error measure. However, finding the optimal bandwidth values by cross-validation can be computationally intensive, especially when p is not small. If good estimates of bandwidth values are available, for example, from the analysis of a similar dataset, the bandwidth values can be specified explicitly to save time.

`reltol` specifies the relative convergence tolerance when choosing the bandwidth values (`bw`). It will be passed on to `stats::optim()`. For most analyses, the default value of $1e-4$ provides reasonably good results. A smaller value such as $1e-5$ or $1e-6$ could be used for further improvement at the cost of more computation time.

Value

<code>fdr</code>	a vector of local FDR estimates. <code>fdr[i]</code> is the posterior probability of the i th null hypothesis is true given all the data. $1-fdr[i]$ is the posterior probability of being a signal (the corresponding null hypothesis is false).
<code>FDR</code>	a vector of FDR values (q-values), which can be used to control FDR at a certain level by thresholding the FDR values.
<code>pi0</code>	a vector of true null probability estimates. This contains the prior probabilities of being null.
<code>bw</code>	a vector of bandwidths for conditional alternative density estimation
<code>fit.gam</code>	an object of <code>mgcv::gam</code>

Author(s)

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References

Liang (2019), Empirical Bayes analysis of RNA sequencing experiments with auxiliary information, to appear in Annals of Applied Statistics

Examples

```
data(pso)
ind.nm <- is.na(pso$tval_mic)
x <- pso$len_gene[ind.nm]
# normalize covariate
x <- rank(x)/length(x)
y <- pso$zval[ind.nm]
# assign names to the z-values helps to give names to the output variables
names(y) <- row.names(pso)[ind.nm]

fit.nm <- CLfdr(x=x, y=y)
fit.nm$fdr[1:5]
```

EstFDR	<i>FDR estimation</i>
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Description

False discovery rate (FDR) estimation from local FDR

Usage

```
EstFDR(fdr)
```

Arguments

fdr vector of local FDR

Value

the estimate of the FDR

Examples

```
lfdr <- c(runif(900), rbeta(100, 1, 10))
FDR <- EstFDR(lfdr)
sum(FDR < 0.05)
```

EstNullProp_RB	<i>Right-boundary procedure</i>
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Description

True null proportion (π_0) estimator of Liang and Nettleton (2012), JRSSB

Usage

```
EstNullProp_RB(pval, lambda.vec = 0.05 * seq_len(19))
```

Arguments

pval vector of p-values
lambda.vec vector of lambda candidates (excluding 0 and 1)

Value

the estimate of the overall true null proportion

Examples

```
pval <- c(runif(900), rbeta(100, 1, 10))
EstNullProp_RB(pval)
```

pso

Psoriasis RNA-seq dataset

Description

A dataset containing the test statistics to analyze an RNA-seq study of psoriasis.

Usage

pso

Format

A dataset with the following vectors:

zval 16490 z-values of genes with matching microarray data

len_gene 16490 gene coding region length for zval

tval_mic 16490 matching microarray t-statistics

Source

Liang (2019), Empirical Bayes analysis of RNA sequencing experiments with auxiliary information, to appear in *Annals of Applied Statistics*;

Examples

```
data(pso)
dim(pso)
# total number of genes without matching microarray data
sum(is.na(pso$tval_mic))
```

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