Package 'calm'

April 15, 2020

Type Package

Title Covariate Assisted Large-scale Multiple testing

Version 1.0.0

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)

Encoding UTF-8

LazyData false

Imports mgcv, stats, graphics

Suggests knitr, rmarkdown

VignetteBuilder knitr

biocViews Bayesian, DifferentialExpression, GeneExpression, Regression, Microarray, Sequencing, RNASeq, MultipleComparison, Genetics, ImmunoOncology, Metabolomics, Proteomics, Transcriptomics

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BugReports https://github.com/k22liang/calm/issues

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R topics documented:

`calm` *Covariate Assisted Large-scale Multiple testing*

Description

Statistical methods for multiple testing with covariate information.

Details

Package:	calm
Type:	Package
Version:	0.9.0
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License:	GPL (>= 2)
LazyLoad:	yes

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 computed the overall true null proportion when pi0.method="RB".
pi0.method	method to estimate the overall true null proportion (pi0). "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 esitmating bandwidth.
check.gam	indicator to perform gam.check function on the nonparametric fit.
k.gam	tuning parameter for mgcv::gam.
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

fdr	a vector of local FDR estimates. fdr[i] is the posteiror probability of the ith 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).
FDR	a vector of FDR values (q-values), which can be used to control FDR at a certain level by thresholding the FDR values.
pi0	a vector of true null probability estimates. This contains the prior probabilities of being null.
bw	a vector of bandwidths for conditional alternative density estimation
fit.gam	an object of mgcv::gam

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 *FDR estimation*

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 *Right-boundary procedure*

Description

True null proportion (pi_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)
```

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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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