

Package ‘bacon’

October 14, 2021

Type Package

Title Controlling bias and inflation in association studies using the empirical null distribution

Version 1.20.0

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Description Bacon can be used to remove inflation and bias often observed in epigenome- and transcriptome-wide association studies. To this end bacon constructs an empirical null distribution using a Gibbs Sampling algorithm by fitting a three-component normal mixture on z-scores.

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Depends R (>= 3.3), methods, stats, ggplot2, graphics, BiocParallel, ellipse

Suggests BiocStyle, knitr, rmarkdown, testthat, roxygen2

biocViews ImmunoOncology, StatisticalMethod, Bayesian, Regression, GenomeWideAssociation, Transcriptomics, RNASeq, MethylationArray, BatchEffect, MultipleComparison

RoxygenNote 6.1.1

Collate 'BaconClass.R' 'BaconMethods.R' 'bacon.R' 'normmixture.R'

VignetteBuilder knitr

NeedsCompilation yes

git_url <https://git.bioconductor.org/packages/bacon>

git_branch RELEASE_3_13

git_last_commit 629e321

git_last_commit_date 2021-05-19

Date/Publication 2021-10-14

R topics documented:

bacon	2
Bacon-class	4
bias	4
dnormmix	5
es	6
estimates	6
fit	7
inflation	8
meta	9
plot,Bacon-method	10
plotnormmix	10
posteriors	11
pval	12
rnormmix	13
se	13
topTable	14
traces	15
tstat	16
Index	17

bacon

*Gibbs sampler***Description**

Gibbs Sampler Algorithm to fit a three component normal mixture to z-scores

Usage

```
bacon(teststatistics = NULL, effectsizes = NULL,
      standarderrors = NULL, niter = 5000L, nburnin = 2000L,
      nbins = 1000, trim = 0.999, level = 0.05, na.exclude = FALSE,
      verbose = FALSE, priors = list(sigma = list(alpha = 1.28, beta =
      0.36), mu = list(lambda = c(0, 3, -3), tau = c(1000, 100, 100)), epsilon
      = list(gamma = c(90, 5, 5)))
```

Arguments

teststatistics	numeric vector or matrix of test-statistics
effectsizes	numeric vector or matrix of effect-sizes
standarderrors	numeric vector or matrix of standard errors
niter	number of iterations
nburnin	length of the burnin period
nbins	default 1000 else bin test-statistics

trim	default 0.999 trimming test-statistics
level	significance level used to determine prop. null for starting values
na.exclude	see ?na.exclude
verbose	default FALSE
priors	list of parameters of for the prior distributions

Value

object of class-Bacon

Author(s)

mvaniterson

References

Implementation is based on a version from Zhihui Liu <https://macsphere.mcmaster.ca/handle/11375/9368>

Examples

```
##simulate some test-statistic from a normal mixture
##and run bacon
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
bc <- bacon(y)
##extract all estimated mixture parameters
estimates(bc)
##extract inflation
inflation(bc)
##extract bias
bias(bc)

##extract bias and inflation corrected test-statistics
head(tstat(bc))

##inspect the Gibbs Sampling output
traces(bc)
posteriors(bc)
fit(bc)

##simulate multiple sets of test-statistic from a normal mixture
##and run bacon
y <- matrix(rnormmix(10*2000, c(0.9, 0, 1, 0, 4, 1)), ncol=10)
bc <- bacon(y)
##extract all estimated mixture parameters
estimates(bc)
##extract only the inflation
inflation(bc)
##extract only the bias
bias(bc)
##extract bias and inflation corrected P-values
```

```
head(pval(bc))
##extract bias and inflation corrected test-statistics
head(tstat(bc))
```

Bacon-class	<i>An S4 class container for storing Gibbs Sampler input and output</i>
-------------	---

Description

An S4 class container for storing Gibbs Sampler input and output

Slots

teststatistics numeric vector or matrix of test-statistics
 effectsizes numeric vector or matrix of effect-sizes
 standarderrors numeric vector or matrix of standard errors
 traces array of Gibbs Sampler traces
 estimates vector or matrix of parameter estimates
 priors list of parameters of for the prior distributions
 niter number of iterations
 nburnin length of the burnin period

bias	<i>Method to extract the estimated bias from the 'bacon'-object</i>
------	---

Description

Method to extract the estimated bias from the 'bacon'-object

Usage

```
bias(object)

## S4 method for signature 'Bacon'
bias(object)
```

Arguments

object 'bacon'-object

Value

vector or matrix of inflation

See Also[bacon](#)**Examples**

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
bias(bc)
```

dnormmix*density of a k-component normal mixture*

Description

density of a k-component normal mixture

Usage

```
dnormmix(x, theta)
```

Arguments

x	x like dnorm(x, ...
theta	parameters of the mixture proportion, mean and sd

Details

details follow

Value

density of a k-component normal mixture

Author(s)

mvaniterson

Examples

```
n <- 2000
theta <- c(0.8, 0, 1, 0, 4, 1)
x <- rnormmix(n, theta)
hist(x, freq=FALSE, n=100)
curve(dnormmix(x, theta), add=TRUE, lwd=2)
```

es *Method to extract inflation- and bias-corrected effect-sizes*

Description

Method to extract inflation- and bias-corrected effect-sizes

Usage

```
es(object, corrected = TRUE)

## S4 method for signature 'Bacon'
es(object, corrected = TRUE)
```

Arguments

object	'bacon'-object
corrected	optional return uncorrected

Value

vector or matrix of effect-sizes

See Also

[bacon](#)

Examples

```
es <- replicate(6, rnormmix(2000, c(0.9, 0, 1, 0, 4, 1)))
se <- replicate(6, 0.8*sqrt(4/rchisq(2000,df=4)))
bc <- bacon(NULL, es, se)
head(es(bc))
```

estimates *Method to extract the estimated parameters from the 'bacon'-object*

Description

Method to extract the estimated parameters from the 'bacon'-object

Usage

```
estimates(object)

## S4 method for signature 'Bacon'
estimates(object)
```

Arguments

object 'bacon'-object

Value

vector or matrix of estimates

See Also

[bacon](#)

Examples

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
estimates(bc)
```

fit

Method to plot mixture fit

Description

Method to plot mixture fit

Usage

```
fit(object, index = 1, ...)
```

S4 method for signature 'Bacon'

```
fit(object, index, col = "grey75", border = "grey75",
    ...)
```

Arguments

object 'bacon'-object

index if multiple sets of test-statistics where provided

... additional plotting parameters

col line color default 'grey75'

border border color 'grey75'

Value

plot of the Gibbs Sampler mixture fit

See Also[bacon](#)**Examples**

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
fit(bc)
```

inflation*Method to extract the estimated inflation from the 'bacon'-object*

Description

Method to extract the estimated inflation from the 'bacon'-object

Usage

```
inflation(object)
```

```
## S4 method for signature 'Bacon'
inflation(object)
```

Arguments

object 'bacon'-object

Value

vector or matrix of inflation

See Also[bacon](#)**Examples**

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
inflation(bc)
```

meta	<i>fixed meta-analysis</i>
------	----------------------------

Description

Perform fixed meta-analysis using inflation and bias corrected effect-sizes and standard errors

Usage

```
meta(object, corrected = TRUE, ...)  
  
## S4 method for signature 'Bacon'  
meta(object, corrected = TRUE, ...)
```

Arguments

object	'bacon'-object
corrected	optional return uncorrected
...	additional arguments

Details

TODO maybe add idea's from http://www.netstorm.be/home/meta_analysis#metaAnalysisU

Value

object of class 'bacon' with added fixed-effect meta-analysis test-statistics, effect-sizes and standard-errors

See Also

[bacon](#)

Examples

```
es <- replicate(6, rnormmix(2000, c(0.9, 0, 1, 0, 4, 1)))  
se <- replicate(6, 0.8*sqrt(4/rchisq(2000,df=4)))  
bc <- bacon(NULL, es, se)  
mbc <- meta(bc)
```

plot,Bacon-method *plot hist or qq*

Description

simple ggplot2 plotting function for 'bacon'-object

Usage

```
## S4 method for signature 'Bacon'
plot(x, y, type = c("hist", "qq"))
```

Arguments

x	'bacon'-object
y	NULL
type	hist or qq

Value

either qq-plot of P-values or histogram of Test-statistics

plotnormmix *plot normal mixtures*

Description

plot normal mixtures

Usage

```
plotnormmix(x, theta, ...)
```

Arguments

x	vector of test statistics
theta	parameters describing the mixture components
...	arguments passed to hist

Details

details follow

Value

return plot with histogram of the data and mixture and individual components

Author(s)

mvaniterson

Examples

```
n <- 2000
theta <- c(0.8, 0, 1, 0, 4, 1)
x <- rnormmix(n, theta)
plotnormmix(x, theta)
```

posterior*Method to plot posterior distribution*

Description

Method to plot posterior distribution

Usage

```
posterior(object, thetas = c("sigma.0", "p.0"), index = 1,
  alphas = c(0.95, 0.9, 0.75), xlab = "", ylab = "", ...)

## S4 method for signature 'Bacon'
posterior(object, thetas = c("sigma.0", "p.0"),
  index = 1, alphas = c(0.95, 0.9, 0.75), xlab = "", ylab = "",
  ...)
```

Arguments

object	'bacon'-object
thetas	which thetas to plot
index	if multiple sets of test-statistics where provided
alphas	significance level confidence ellipses
xlab	optional xlab
ylab	optional ylab
...	additional plotting parameters

Value

plot of the Gibbs Sampler posterior probabilities

See Also[bacon](#)

Examples

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
posteriors(bc)
```

pval

Method to extract inflation- and bias-corrected P-values

Description

Method to extract inflation- and bias-corrected P-values

Usage

```
pval(object, corrected = TRUE)

## S4 method for signature 'Bacon'
pval(object, corrected = TRUE)
```

Arguments

object	'bacon'-object
corrected	optional return uncorrected

Value

vector or matrix of P-values

See Also

[bacon](#)

Examples

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
bc <- bacon(y, nbins=100) #nbins = 100 to speed up the calculations
head(pval(bc))
```

rnormmix	<i>sample from a normal mixture</i>
----------	-------------------------------------

Description

sample from a normal mixture

Usage

```
rnormmix(n, theta, shuffle = TRUE)
```

Arguments

n	size
theta	parameters
shuffle	shuffle return vectors or keep nulls and alternative ordered (null, alts)

Details

details follow

Value

n samples from a normal mixture with parameters theta

Author(s)

mvaniterson

Examples

```
n <- 2000
theta <- c(0.8, 0, 1, 0, 4, 1)
x <- rnormmix(n, theta)
```

se	<i>Method to extract inflation- and bias-corrected standard errors</i>
----	--

Description

Method to extract inflation- and bias-corrected standard errors

Usage

```
se(object, corrected = TRUE)

## S4 method for signature 'Bacon'
se(object, corrected = TRUE)
```

Arguments

```
object          'bacon'-object
corrected       optional return uncorrected
```

Value

vector or matrix of standard-errors

See Also

[bacon](#)

Examples

```
es <- replicate(6, rnormmix(2000, c(0.9, 0, 1, 0, 4, 1)))
se <- replicate(6, 0.8*sqrt(4/rchisq(2000,df=4)))
bc <- bacon(NULL, es, se)
head(se(bc))
```

topTable

topTable

Description

Extract top features after meta analysis

Usage

```
topTable(object, number = 10, adjust.method = "bonf",
          sort.by = c("pval", "eff.size"))

## S4 method for signature 'Bacon'
topTable(object, number = 10, adjust.method = "bonf",
          sort.by = c("pval", "eff.size"))
```

Arguments

```
object          'bacon'-object
number          return specified number of top features, n=-1 return all features
adjust.method   P-value multiple testing adjustment method default bonferroni
sort.by        order results by pval or eff.size
```

Value

table with top features

See Also

[bacon](#)

Examples

```
es <- replicate(6, rnormmix(2000, c(0.9, 0, 1, 0, 4, 1)))
se <- replicate(6, 0.8*sqrt(4/rchisq(2000,df=4)))
bc <- bacon(NULL, es, se)
mbc <- meta(bc)
topTable(mbc)
```

traces

Method to plot Gibbs sampling traces

Description

Method to plot Gibbs sampling traces

Usage

```
traces(object, burnin = TRUE, index = 1)
```

```
## S4 method for signature 'Bacon'
traces(object, burnin = TRUE, index = 1)
```

Arguments

object	'bacon'-object
burnin	include burnin period default true
index	if multiple sets of test-statistics where provided

Value

plot of the Gibbs Sampler traces

See Also

[bacon](#)

Examples

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))
##nbins = 100 to speed up the calculations
bc <- bacon(y, nbins=100)
traces(bc)
```

tstat	<i>Method to extract inflation- and bias-corrected test-statistics</i>
-------	--

Description

Method to extract inflation- and bias-corrected test-statistics

Usage

```
tstat(object, corrected = TRUE)
```

```
## S4 method for signature 'Bacon'  
tstat(object, corrected = TRUE)
```

Arguments

object	'bacon'-object
corrected	optional return uncorrected

Value

vector or matrix of test-statistics

See Also

[bacon](#)

Examples

```
y <- rnormmix(2000, c(0.9, 0, 1, 0, 4, 1))  
##nbins = 100 to speed up the calculations  
bc <- bacon(y, nbins=100)  
head(tstat(bc))
```


Index

bacon, [2](#), [5–9](#), [11](#), [12](#), [14–16](#)
Bacon-class, [4](#)
bias, [4](#)
bias, Bacon-method (bias), [4](#)

dnormmix, [5](#)

es, [6](#)
es, Bacon-method (es), [6](#)
estimates, [6](#)
estimates, Bacon-method (estimates), [6](#)

fit, [7](#)
fit, Bacon-method (fit), [7](#)

inflation, [8](#)
inflation, Bacon-method (inflation), [8](#)

meta, [9](#)
meta, Bacon-method (meta), [9](#)

plot, Bacon-method, [10](#)
plotnormmix, [10](#)
posteriors, [11](#)
posteriors, Bacon-method (posteriors), [11](#)
pval, [12](#)
pval, Bacon-method (pval), [12](#)

rnormmix, [13](#)

se, [13](#)
se, Bacon-method (se), [13](#)

topTable, [14](#)
topTable, Bacon-method (topTable), [14](#)
traces, [15](#)
traces, Bacon-method (traces), [15](#)
tstat, [16](#)
tstat, Bacon-method (tstat), [16](#)