Package 'bacon'

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Type Package

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

Version 1.40.0

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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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Encoding UTF-8

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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))),
  globalSeed = 42,
  parallelSeed = 42
)
```

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 for the prior distributions
globalSeed	default 42 global seed. If set to NULL, randomization will occur for sequential and parallel bacon calls
parallelSeed	default 42 BiocParallel RNGseed. If input statistics are a matrix and globalSeed=NULL, setting parallelSeed=NULL will allow randomization across parallel processes within a bacon call and across separate calls to bacon.

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` *An S4 class container for storing Gibbs Sampler input and output*

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

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-statsistics 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 *fixed meta-analysis*

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)
```

posteriors *Method to plot posterior distribution*

Description

Method to plot posterior distribution

Usage

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

## S4 method for signature 'Bacon'
posteriors(
  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-statsistics 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 *sample from a normal mixture*

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 *Method to extract inflation- and bias-corrected standard errors*

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-statsistics 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` *Method to extract inflation- and bias-corrected test-statistics*

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))
```

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