

# Package ‘episcan’

September 15, 2018

**Title** Scan Pairwise Epistasis

**Version** 0.0.1

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**Description** Searching genomic interactions with linear/logistic regression in a high-dimensional dataset is a time-consuming task. This package provides some efficient ways to scan epistasis in genome-wide interaction studies (GWIS). Both case-control status (binary outcome) and quantitative phenotype (continuous outcome) are supported (the main references: 1. Kam-Thong, T., D. Czamara, K. Tsuda, K. Borgwardt, C. M. Lewis, A. Erhardt-Lehmann, B. Hemmer, et al. (2011). <doi:10.1038/ejhg.2010.196>. 2. Kam-Thong, T., B. Pütz, N. Karbalai, B. Müller-Myhsok, and K. Borgwardt. (2011). <doi:10.1093/bioinformatics/btr218>.)

**Depends** R (>= 3.5.0)

**License** GPL (>= 2)

**Encoding** UTF-8

**Suggests** testthat, knitr, rmarkdown

**VignetteBuilder** knitr

**LazyData** true

**RoxygenNote** 6.1.0

**NeedsCompilation** no

**Repository** CRAN

**Date/Publication** 2018-09-14 23:02:19 UTC

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checkchunksize	<i>Check chunk size</i>
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### Description

Check the chunk size whether it is over the given number of variables(vaiaants) in genotype data. If yes, reset the chunk size equal to the number of variables(vaiaants).

### Usage

```
checkchunksize(c, m, n = NULL, ...)
```

### Arguments

c	an integer indicating the set chunk size.
m	an integer indicating the number of variables(vaiaants) in geno1 if there is only one genotype input.
n	an integer indicating the number of variables(vaiaants) in geno2 if there are two genotype inputs. The default is NULL.
...	not used.

### Value

an integer indicating the chunk size

### Examples

```
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)),
ncol = 10)
geno2 <- matrix(sample(0:2, size = 2000, replace = TRUE, prob = c(0.4, 0.3, 0.3)),
ncol = 20)

# if chunk size is smaller, there is no problem
chunksize <- 10
checkchunksize(chunksize, ncol(geno1))

# if chunk size is bigger than the number of columns in genotype input,
# set chunk size equal to the number of columns in genotype input
chuksize <- 12
```

```

checkchunksize(chunksize, ncol(geno1))

# if chunk size is bigger than the number of columns of geno1 and geno2,
# set chunk size equal to the minima number of columns of geno1 and geno2
chunksize <- 50
checkchunksize(chunksize, ncol(geno1), ncol(geno2))

```

---

epiblaster1geno	<i>Parallelized calculation of the difference of correlation coefficients and compute Z test with one genotype input</i>
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---

## Description

Calculate the difference of correlation coefficients between cases and controls, conduct  $Z$  test for the differences (values) and choose variant pairs with the significance below the given threshold for output.

## Usage

```

epiblaster1geno(geno, pheno, chunk = 1000, zpthres = 1e-05,
  outfile = "NONE", suffix = ".txt", ...)

```

## Arguments

geno	is the normalized genotype data. It can be a matrix or a dataframe, or a big.matrix object (from <b>bigmemory</b> ). The columns contain the information of variables and the rows contain the information of samples.
pheno	a vector containing the binary phenotype information (case/control). The values are either 0 (control) or 1 (case).
chunk	is the number of variants in each chunk. Default: 1000.
zpthres	is the significance threshold to select variant pairs for output. Default is 1e-6.
outfile	is the base of out filename. Default: 'NONE'.
suffix	is the suffix of out filename. Default: '.txt'.
...	not used.

## Value

null

## Examples

```

# simulate some data
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)), ncol = 10)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)), col = paste0("rs", 1:ncol(geno1)))
p1 <- c(rep(0, 60), rep(1, 40))

```

```

# normalized data
geno1 <- scale(geno1)

# one genotype with case-control phenotype
epiblaster1geno(geno = geno1,
pheno = p1,
outfile = "episcan_1geno_cc",
suffix = ".txt",
zpthres = 0.9,
chunk = 10)

# take a look at the result
res <- read.table("episcan_1geno_cc.txt",
header = TRUE,
stringsAsFactors = FALSE)
head(res)

```

---

epiblaster2genos	<i>Parallelized calculation of the difference of correlation coefficients and compute Z test with two genotype inputs</i>
------------------	---

---

## Description

Calculate the difference of correlation coefficients between cases and controls, conduct Z test for the differences (values) and choose variant pairs with the significance below the given threshold for output.

## Usage

```
epiblaster2genos(geno1, geno2, pheno, chunk = 1000, zpthres = 1e-05,
  outfile = "NONE", suffix = ".txt", ...)
```

## Arguments

geno1	is the first normalized genotype data. It can be a matrix or a dataframe, or a <b>big.matrix</b> object from <b>bigmemory</b> . The columns contain the information of variables and the rows contain the information of samples.
geno2	is the second normalized genotype data. It can be a matrix or a dataframe, or a <b>big.matrix</b> object from <b>bigmemory</b> . The columns contain the information of variables and the rows contain the information of samples.
pheno	a vector containing the binary phenotype information (case/control). The values are either 0 (control) or 1 (case).
chunk	is the number of variants in each chunk.
zpthres	is the significance threshold to select variant pairs for output. Default is 1e-6.
outfile	is the prefix of out filename.
suffix	is the suffix of out filename.
...	not used.

**Value**

null

**Examples**

```
# simulate some data
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)), ncol = 10)
geno2 <- matrix(sample(0:2, size = 2000, replace = TRUE, prob = c(0.4, 0.3, 0.3)), ncol = 20)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)), col = paste0("rs", 1:ncol(geno1)))
dimnames(geno2) <- list(row = paste0("IND", 1:nrow(geno2)), col = paste0("exm", 1:ncol(geno2)))
p1 <- c(rep(0, 60), rep(1, 40))

# normalized data
geno1 <- scale(geno1)
geno2 <- scale(geno2)

# two genotypes with quantitative phenotype
epiblaster2genos(geno1 = geno1,
  geno2 = geno2,
  pheno = p1, outfile = "episcan_2geno_cc",
  suffix = ".txt",
  zpthres = 0.9,
  chunk = 10)

# take a look at the result
res <- read.table("episcan_2geno_cc.txt",
  header = TRUE,
  stringsAsFactors = FALSE)
head(res)
```

---

epiHSIC

*Calculate HSIC values*

---

**Description**

Calculate HSIC values

**Usage**

```
epiHSIC(A = NULL, B = NULL, P = NULL, ...)
```

**Arguments**

A	is one matrix.
B	is one matrix.
P	is "phenoype", a vector.
...	not used.

**Value**

a matrix

**Author(s)**

Beibei Jiang <beibei\_jiang@psych.mpg.de>

**Examples**

```
# simulate some data
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)), ncol = 10)
geno2 <- matrix(sample(0:2, size = 2000, replace = TRUE, prob = c(0.4, 0.3, 0.3)), ncol = 20)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)), col = paste0("rs", 1:ncol(geno1)))
dimnames(geno2) <- list(row = paste0("IND", 1:nrow(geno2)), col = paste0("exm", 1:ncol(geno2)))

epiHSIC(A = scale(geno1),
        B = scale(geno2),
        P = rnorm(100))
```

---

epiHSIC1geno

*Calculate epistasis using HSIC with one genotype input*

---

**Description**

Calculate the significance of epistasis according the definition of HSIC, conduct  $Z$  test for HSIC values and choose variant pairs with the significance below the given threshold for output.

**Usage**

```
epiHSIC1geno(geno = NULL, pheno, chunk = 1000, zpthres = 1e-05,
             outfile = "NONE", suffix = ".txt", ...)
```

**Arguments**

geno	is the normalized genotype data. It can be a matrix or a dataframe, or a big.matrix object from <b>bigmemory</b> . The columns contain the information of variables and the rows contain the information of samples.
pheno	is a vector containing the normalized phenotype information.
chunk	is the number of variants in each chunk.
zpthres	is is the significance threshold to select variant pairs for output. Default is 1e-6.
outfile	is the basename of out filename.
suffix	is the suffix of out filename.
...	not used.

**Value**

null

**Author(s)**

Beibei Jiang <beibei\_jiang@psych.mpg.de>

**Examples**

```
# simulate some data
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)), ncol = 10)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)), col = paste0("rs", 1:ncol(geno1)))
p2 <- rnorm(100, mean = 5, sd = 10)

# normalized data
geno1 <- scale(geno1)
p2 <- as.vector(unlist(scale(p2)))

# one genotypes with quantitative phenotype
epiHSIC1geno(geno = geno1,
             pheno = p2,
             outfile = "episcan_1geno_quant",
             suffix = ".txt",
             zpthres = 0.9,
             chunk = 10)

# take a look at the result
res <- read.table("episcan_1geno_quant.txt",
                 header = TRUE,
                 stringsAsFactors = FALSE)
head(res)
```

---

epiHSIC2genos

*Calculate epistasis using HSIC with two genotype inputs*

---

**Description**

Calculate the significance of epistasis according the definition of HSIC, conduct Z test for HSIC values and choose variant pairs with the significance below the given threshold for output.

**Usage**

```
epiHSIC2genos(geno1 = NULL, geno2 = NULL, pheno = NULL,
              chunk = 1000, zpthres = 1e-05, outfile = "NONE", suffix = ".txt",
              ...)
```

**Arguments**

geno1	is the first normalized genotype data. It can be a matrix or a dataframe, or a big.matrix object from <b>bigmemory</b> . The columns contain the information of variables and the rows contain the information of samples.
geno2	is the second normalized genotype data. It can be a matrix or a dataframe, or a big.matrix object from <b>bigmemory</b> . The columns contain the information of variables and the rows contain the information of samples.
pheno	is a vector containing the normalized phenotype information.
chunk	is the number of variants in each chunk.
zpthres	is the significance threshold for cut-off output of the variant pairs.
outfile	is the basename of out filename.
suffix	is the suffix of out filename.
...	not used

**Value**

null

**Examples**

```
# simulate some data
set.seed(123)
n1 <- 10; n2 <- 15; rows <- 10
geno1 <- matrix(sample(0:2, size = n1*rows, replace = TRUE, prob = c(0.5, 0.3, 0.2)), ncol = n1)
geno2 <- matrix(sample(0:2, size = n2*rows, replace = TRUE, prob = c(0.4, 0.3, 0.3)), ncol = n2)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)), col = paste0("rs", 1:ncol(geno1)))
dimnames(geno2) <- list(row = paste0("IND", 1:nrow(geno2)), col = paste0("exm", 1:ncol(geno2)))
p2 <- rnorm(rows, mean = 5, sd = 10)

# normalized data
geno1 <- scale(geno1)
geno2 <- scale(geno2)
p2 <- as.vector(unlist(scale(p2)))

# two genotypes with quantitative phenotype
epiHSIC2genos(geno1 = geno1,
              geno2 = geno2,
              pheno = p2,
              outfile = "episcan_2geno_quant",
              suffix = ".txt",
              zpthres = 0.9,
              chunk = 10)

# take a look at the result
res <- read.table("episcan_2geno_quant.txt",
                 header = TRUE,
                 stringsAsFactors = FALSE)
head(res)
```



---

 episcan

*Scan pairwise epistasis*


---

### Description

Genomic interaction analysis with EPIBLASTER or epistasis-oriented Hilbert–Schmidt Independence Criterion (HSIC).

### Usage

```
episcan(geno1, geno2 = NULL, pheno = NULL,
        phetype = c("case-control", "quantitative"), outfile = "episcan",
        suffix = ".txt", zpthres = 1e-06, chunksize = 1000, scale = TRUE,
        ...)
```

### Arguments

geno1	a data.frame or matrix of the first genotype data. <b>big.matrix</b> object from <b>bigmemory</b> also works. The columns contain the information of variables and the rows contain the information of samples.
geno2	optional. A data.frame or matrix of the second genotype data. <b>big.matrix</b> object from <b>bigmemory</b> also works. The columns contain the information of variables and the rows contain the information of samples.
pheno	a vector (named or not). If not provided, the value of geno2 will be used if it is a vector. The values is either case-control phenotype (0, 1) or quantitative phenotype.
phetype	character string. Either "case-control" or "quantitative".
outfile	output file name. Default is "episcan".
suffix	suffix for output file. Default is ".txt". The final result will be stored in <code>outfile</code> <code>suffix</code> .
zpthres	is the significance threshold to select variant pairs for output. Default is 1e-6.
chunksize	the number of variants in each chunk.
scale	a logical value to define wheter the input data needs to be normalized. Default is TRUE which means, by default, all the genotype data will be normalized and if the phetype is "quantitative", the phenotype will also be normalized.
...	not used.

### Value

null

### Author(s)

Beibei Jiang <beibei\_jiang@psych.mpg.de>

## References

Kam-Thong, T., D. Czamara, K. Tsuda, K. Borgwardt, C. M. Lewis, A. Erhardt-Lehmann, B. Hemmer, et al. 2011. "EPIBLASTER-Fast Exhaustive Two-Locus Epistasis Detection Strategy Using Graphical Processing Units." *Journal Article*. *European Journal of Human Genetics* 19 (4): 465–71. <https://doi.org/10.1038/ejhg.2010.196>.

Kam-Thong, T., B. Pütz, N. Karbalai, B. Müller-Myhsok, and K. Borgwardt. 2011. "Epistasis Detection on Quantitative Phenotypes by Exhaustive Enumeration Using GPUs." *Journal Article*. *Bioinformatics* 27 (13): i214–21. <https://doi.org/10.1093/bioinformatics/btr218>.

## Examples

```
# simulate some data
set.seed(123)
geno1 <- matrix(sample(0:2, size = 1000, replace = TRUE, prob = c(0.5, 0.3, 0.2)),
ncol = 10)
geno2 <- matrix(sample(0:2, size = 2000, replace = TRUE, prob = c(0.4, 0.3, 0.3)),
ncol = 20)
dimnames(geno1) <- list(row = paste0("IND", 1:nrow(geno1)),
col = paste0("rs", 1:ncol(geno1)))
dimnames(geno2) <- list(row = paste0("IND", 1:nrow(geno2)),
col = paste0("exm", 1:ncol(geno2)))
p1 <- c(rep(0, 60), rep(1, 40))
p2 <- rnorm(100)

# one genotype with case-control phenotype
episcan(geno1 = geno1,
geno2 = NULL,
pheno = p1,
phetype = "case-control",
outfile = "episcan_1geno_cc",
suffix = ".txt",
zpthres = 0.9,
chunksize = 10,
scale = TRUE)

# take a look at the result
res <- read.table("episcan_1geno_cc.txt",
header = TRUE,
stringsAsFactors = FALSE)
head(res)

# two genotypes with quantitative phenotype
episcan(geno1 = geno1,
geno2 = geno2,
pheno = p2,
phetype = "quantitative",
outfile = "episcan_2geno_quant",
suffix = ".txt",
zpthres = 0.9,
chunksize = 10,
scale = TRUE)
```

---

getcor	<i>Get correlation matrix</i>
--------	-------------------------------

---

**Description**

Fast calculation of correlation matrix on CPU (the idea is from **WGCNA** fast function for pearson correlations)

**Usage**

```
getcor(A = NULL, B = NULL, method = "pearson", ...)
```

**Arguments**

A	is a matrix or data.frame.
B	is a matrix or data.frame.
method	a character string indicating which correlation coefficient is to be computed. Current version only supports "pearson" correlation.
...	not used.

**Value**

correlation matrix

**Author(s)**

Beibei Jiang <beibei\_jiang@psych.mpg.de>

**Examples**

```
set.seed(123)
A <- matrix(rnorm(100, mean = 5, sd = 10), ncol = 10)
B <- matrix(rnorm(200, mean = 10, sd = 100), ncol = 20)
C <- getcor(A, B)
```

---

ithChunk	<i>index set for idx-th chunk of size chunk for n elements</i>
----------	--

---

**Description**

For proper use of this function it will return the set of variant indices corresponding to the `idx`-th chunk of size `chunk` in `n` variants, taking care of the case that the last chunk might have less than `n` elements. If used with an `idx`-value outside the possible chunks (i.e., negative or larger than `ceiling(n/chunk)`) an empty vector (`numeric(0)`) is returned.

**Usage**

```
ithChunk(idx, n, chunk = 1000)
```

**Arguments**

idx	chunk index (which chunk, first is 1)
n	total number of variants
chunk	desired chunksize

**Value**

index range into variants for chunk idx (see details)

---

WriteSnpPairs	<i>Write out epistasis result (normal matrix)</i>
---------------	---

---

**Description**

Write out the result of epistasis analysis. Z score matrix is not a symmetric matrix.

**Usage**

```
WriteSnpPairs(Zmatrix, indexArr, outfile = "NONE", ...)
```

**Arguments**

Zmatrix	is the Z score matrix (non-symmetric matrix).
indexArr	is the index of Zmatrix whose z score is over the given zpthres.
outfile	is the SNP pairs file for the second stage.
...	not used.

**Value**

null

**Author(s)**

Beibei Jiang <beibei\_jiang@psych.mpg.de>

---

WriteSnPairs\_sym      *Write out epistasis result (symmetric matrix)*

---

**Description**

Write out the result of epistasis analysis. Z score matrix is a symmetric matrix.

**Usage**

```
WriteSnPairs_sym(Zmatrix, indexArr, outfile = "NONE", ...)
```

**Arguments**

Zmatrix	is the Z score matrix (symmetric matrix).
indexArr	is the index of Zmatrix whose z score is over the given zpthres.
outfile	is the SNP pairs file for the second stage.
...	not used.

**Value**

null

**Author(s)**

Beibei Jiang <beibei\_jiang@psych.mpg.de>

---

ZtoP      *Convert Z-score to corresponding p-value*

---

**Description**

Convert Z score to corresponding p-values

**Usage**

```
ZtoP(z.score, ...)
```

**Arguments**

z.score	Z-score(s) (either scalar or vector).
...	not used.

**Value**

corresponding p-value(s).

**Note**

Due to the IEEE number limits of representing doubles, any  $Z$  score over 37.5192999999999765 will be converted to a  $p$ -value of  $1e-309$ .

**Author(s)**

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