

Package ‘AlphaBeta’

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Type Package

Title Computational inference of epimutation rates and spectra from high-throughput DNA methylation data in plants

Version 1.0.0

Description

AlphaBeta is a computational method for estimating epimutation rates and spectra from high-throughput DNA methylation data in plants.

The method has been specifically designed to:

1. analyze 'germline' epimutations in the context of multi-generational mutation accumulation lines (MA-lines).
2. analyze 'somatic' epimutations in the context of plant development and aging.

License GPL-3

Depends R (>= 3.6.0)

Imports dplyr (>= 0.7), data.table (>= 1.10), stringr (>= 1.3), utils (>= 3.6.0), gtools (>= 3.8.0), optimx (>= 2018-7.10), expm (>= 0.999-4), stats (>= 3.6), BiocParallel (>= 1.18)

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LazyLoad yes

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RoxygenNote 6.1.1

Suggests knitr, rmarkdown

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ABneutral	<i>Run Model with no selection (ABneutral)</i>
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Description

This model assumes that heritable gains and losses in cytosine methylation are selectively neutral.

Usage

```
ABneutral(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir, out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	weight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABneutral RData file.

Examples

```
## Get some toy data
inFile <- system.file("extdata/dm/", "pedigree.csv", package="AlphaBeta")
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))
p0uu_in <- 0.7435074
eqp.weight <- 1
Nstarts <- 2
output.data.dir <- paste0( getwd(), "/" )
out.name <- "CG_global_estimates_ABneutral"
out <- ABneutral(pedigree.data = pedigree,
                 p0uu=p0uu_in,
                 eqp=p0uu_in,
                 eqp.weight=eqp.weight,
                 Nstarts=Nstarts,
                 out.dir=output.data.dir,
                 out.name=out.name)

summary(out)
```

ABneutralSOMA

Model with no selection (outneutral)

Description

This model assumes that somatically heritable gains and losses in cytosine methylation are selectively neutral.

Usage

```
ABneutralSOMA(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir,
              out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	weight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABneutralSoma RData file.

Examples

```

## Get some toy data
inFile <- system.file("extdata/soma/", "pedigreeSoma.csv", package="AlphaBeta")
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))
p0uu_in <- 0.54755
eqp.weight <- 0.001
Nstarts <- 2
output.data.dir <- paste0( getwd(), "/" )
out.name <- "ABneutralSOMA_CG_estimates"
out <- ABneutralSOMA(pedigree.data = pedigree,
                    p0uu=p0uu_in,
                    eqp=p0uu_in,
                    eqp.weight=eqp.weight,
                    Nstarts=Nstarts,
                    out.dir=output.data.dir,
                    out.name=out.name)

summary(out)

```

ABnull

Run model that considers no accumulation of epimutations (ABnull)

Description

Run model that considers no accumulation of epimutations (ABnull)

Usage

```
ABnull(pedigree.data, out.dir, out.name)
```

Arguments

pedigree.data	Generation table name, you can find sample file in
out.dir	outputdirectory
out.name	name of file

Value

ABnull RData file.

Examples

```

# Get some toy data
inFile <- system.file("extdata/dm/", "pedigree.csv", package="AlphaBeta")
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))
output.data.dir <- paste0( getwd(), "/" )
out.name <- "CG_global_estimates_ABnull"
out <- ABnull(pedigree.data = pedigree,
             out.dir=output.data.dir,
             out.name=out.name)

summary(out)

```

ABselectMM	<i>Run model with selection against spontaneous gain of methylation (ABselectMM)</i>
------------	--

Description

This model assumes that heritable losses of cytosine methylation are under negative selection.

Usage

```
ABselectMM(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir,  
           out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	nweight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABselectMM RData file.

Examples

```
## Get some toy data  
inFile <- system.file("extdata/dm/", "pedigree.csv", package="AlphaBeta")  
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))  
p0uu_in <- 0.7435074  
eqp.weight <- 1  
Nstarts <- 2  
output.data.dir <- paste0( getwd(), "/" )  
out.name <- "CG_global_estimates_ABselectMM"  
out <- ABselectMM(pedigree.data = pedigree,  
                 p0uu=p0uu_in,  
                 eqp=p0uu_in,  
                 eqp.weight=eqp.weight,  
                 Nstarts=Nstarts,  
                 out.dir=output.data.dir,  
                 out.name=out.name)  
  
summary(out)
```

ABselectMMSOMA	<i>Model with selection against spontaneous gain of methylation (outselectMM)</i>
----------------	---

Description

This model assumes that somatically heritable gains of cytosine methylation are under negative selection.

Usage

```
ABselectMMSOMA(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir,
  out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	weight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABneutralSoma RData file.

Examples

```
## Get some toy data
inFile <- system.file("extdata/soma/", "pedigreeSoma.csv", package="AlphaBeta")
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))
p0uu_in <- 0.54755
eqp.weight <- 0.001
Nstarts <- 2
output.data.dir <- paste0( getwd(), "/" )
out.name <- "ABselectMMSOMA_CG_estimates"
out <- ABselectMMSOMA(pedigree.data = pedigree,
  p0uu=p0uu_in,
  eqp=p0uu_in,
  eqp.weight=eqp.weight,
  Nstarts=Nstarts,
  out.dir=output.data.dir,
  out.name=out.name)

summary(out)
```

ABselectUU	<i>Run model with selection against spontaneous loss of methylation (ABselectUU)</i>
------------	--

Description

This model assumes that heritable gains of cytosine methylation are under negative selection.

Usage

```
ABselectUU(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir,  
           out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	weight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABselectMM RData file.

Examples

```
## Get some toy data  
inFile <- system.file("extdata/dm/", "pedigree.csv", package="AlphaBeta")  
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))  
p0uu_in <- 0.7435074  
eqp.weight <- 1  
Nstarts <- 2  
output.data.dir <- paste0( getwd(), "/")  
out.name <- "CG_global_estimates_ABselectUU"  
out3 <- ABselectUU(pedigree.data = pedigree,  
                  p0uu=p0uu_in,  
                  eqp=p0uu_in,  
                  eqp.weight=eqp.weight,  
                  Nstarts=Nstarts,  
                  out.dir=output.data.dir,  
                  out.name=out.name)  
  
summary(out3)
```

ABselectUUSOMA	<i>Model with selection against spontaneous loss of methylation (outselectUU)</i>
----------------	---

Description

This model assumes that somatically heritable gains of cytosine methylation are under negative selection.

Usage

```
ABselectUUSOMA(pedigree.data, p0uu, eqp, eqp.weight, Nstarts, out.dir,
  out.name)
```

Arguments

pedigree.data	pedigree data.
p0uu	initial proportion of unmethylated cytosines.
eqp	equilibrium proportion of unmethylated cytosines.
eqp.weight	weight assigned to equilibrium function.
Nstarts	iterations for non linear LSQ optimization.
out.dir	output directory.
out.name	output file name.

Value

ABneutralSoma RData file.

Examples

```
## Get some toy data
inFile <- system.file("extdata/soma/", "pedigreeSoma.csv", package="AlphaBeta")
pedigree <- as.matrix(read.table(inFile, sep=",", header=TRUE, stringsAsFactors = FALSE))
p0uu_in <- 0.54755
eqp.weight <- 0.001
Nstarts <- 2
output.data.dir <- paste0( getwd(), "/" )
out.name <- "ABselectUUSOMA_CG_estimates"
out <- ABselectUUSOMA(pedigree.data = pedigree,
  p0uu=p0uu_in,
  eqp=p0uu_in,
  eqp.weight=eqp.weight,
  Nstarts=Nstarts,
  out.dir=output.data.dir,
  out.name=out.name)

summary(out)
```

 BOOTmodel

Bootstrap analysis with the best model

Description

Bootstrap analysis with the best model

Usage

```
BOOTmodel(pedigree.data, Nboot, out.dir, out.name)
```

Arguments

pedigree.data	pedigree data.
Nboot	number of boot.
out.dir	output directory.
out.name	output file name.

Value

bootstrap result.

Examples

```
## Get some toy data
inFile <- system.file("extdata/models/", "CG_global_estimates_ABneutral.Rdata", package="AlphaBeta")
Nboot <- 4
out.dir <- paste0( getwd(), "/" )
out.name <- "Boot_CG_global_estimates_ABneutral"
Bout <- BOOTmodel(pedigree.data=inFile,
                  Nboot=Nboot,
                  out.dir=out.dir,
                  out.name=out.name)

summary(Bout)
```

 convertDMATRIX

convertDMATRIX

Description

calculate divergence times of the pedigree

Usage

```
convertDMATRIX(sample.info, branch.points, dmatrix, design)
```

Arguments

sample.info input file containing information on generation times and pedigree lineages
 branch.points input file containing lineage branch points
 dmatrix input file containing 5mC divergence values for each sample pair
 design "sibling" or "direct"

Value

pedigree

Examples

```
## Get some toy data
file1 <- system.file("extdata/dm/", "sampleInfo.csv", package="AlphaBeta")
file2 <- system.file("extdata/dm/", "branchPoints.csv", package="AlphaBeta")
file3 <- system.file("extdata/dm/", "AB-dMatrix-CG-0.99.csv", package="AlphaBeta")
sample.info <- read.table(file1, sep="\t", header=TRUE, stringsAsFactors = FALSE)
branch.points <- read.table(file2, sep="\t", header=TRUE, stringsAsFactors = FALSE)
dmatrix <- read.table(file3, sep="\t", header=TRUE, stringsAsFactors = FALSE)
pedigree <- convertDMATRIX(sample.info=sample.info,
  branch.points=branch.points, dmatrix=dmatrix, design="sibling")
head(pedigree)
```

dMatrix

Constructing D-Matrices

Description

Estimating epimutation rates from high-throughput DNA methylation data

Usage

```
dMatrix(genTable, cytosine, posteriorMaxFilter)
```

Arguments

genTable Generation table name, you can find sample file in "extdata" called "generations.fn"
 cytosine Type of cytosine (CHH/CHG/CG)
 posteriorMaxFilter Filter value, based on posteriorMax ex: >= 0.95 or 0.99

Value

generating divergence matrices file.

Examples

```
## Get some toy data
file <- system.file("extdata","generations.fn", package="AlphaBeta")
df<-read.csv(file)
df$filename<-sub("^",paste0(dirname(file),"/"),df$filename )
write.csv(df, file = paste0(dirname(file),"/tm_generations.fn"),row.names=FALSE,quote=FALSE)
file <- system.file("extdata","tm_generations.fn", package="AlphaBeta")
dMatrix(file, "CG", 0.99)
```

FtestRSS

*Comparison of different models and selection of best model***Description**

Comparison of different models and selection of best model

Usage

```
FtestRSS(pedigree.select, pedigree.null)
```

Arguments

```
pedigree.select
                pedigree model.
pedigree.null  ABnull pedigree.
```

Value

result of Ftest.

Examples

```
## Get some toy data
file1 <- system.file("extdata/models/","CG_global_estimates_ABneutral.Rdata", package="AlphaBeta")
file2 <- system.file("extdata/models/","CG_global_estimates_ABnull.Rdata", package="AlphaBeta")
out <- FtestRSS(pedigree.select=file1,
                pedigree.null=file2)
```

makePHYLO

*Generating tree pedigree data***Description**

Generating tree pedigree data

Usage

```
makePHYLO(tall, pedigree, sample.info)
```

Arguments

tall total age of the tree.
 pedigree dmatrix file.
 sample.info sample info file.

Value

tree pedigree data file.

Examples

```
## Get some toy data
file1 <- system.file("extdata/soma/", "AB-dMatrix-CG-0.99.csv", package="AlphaBeta")
file2 <- system.file("extdata/soma/", "sampleInfo.csv", package="AlphaBeta")
d.matrix <- read.table(file1, sep="\t", header=TRUE, stringsAsFactors = FALSE)
sample.info <- read.table(file2, sep="\t", header=TRUE, stringsAsFactors = FALSE)
# in our case, the total age of tree is 330
out <- makePHYLO(tall=330, pedigree = d.matrix, sample.info = sample.info)
```

rc.meth.lvl

Calculating rc.Meth.lvl

Description

Estimating epimutation rates from high-throughput DNA methylation data

Usage

```
rc.meth.lvl(genTable, cytosine, posteriorMaxFilter)
```

Arguments

genTable Generation table name, you can find sample file in "extdata" called "generations.fn"
 cytosine Type of cytosine (CHH/CHG/CG)
 posteriorMaxFilter Filter value, based on posteriorMax

Value

rc meth lvl.

Examples

```
## Get some toy data
file <- system.file("extdata", "tm_generations.fn", package="AlphaBeta")
rc.meth.lvl(file, "CG", 0.99)
```

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