Package 'DMCHMM'

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Type Package

Title Differentially Methylated CpG using Hidden Markov Model

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Description A pipeline for identifying differentially methylated CpG sites using Hidden Markov Model in bisulfite sequencing data. DNA methylation studies have enabled researchers to understand methylation patterns and their regulatory roles in biological processes and disease. However, only a limited number of statistical approaches have been developed to provide formal quantitative analysis. Specifically, a few available methods do identify differentially methylated CpG (DMC) sites or regions (DMR), but they suffer from limitations that arise mostly due to challenges inherent in bisulfite sequencing data. These challenges include: (1) that read-depths vary considerably among genomic positions and are often low; (2) both methylation and autocorrelation patterns change as regions change; and (3) CpG sites are distributed unevenly. Furthermore, there are several methodological limitations: almost none of these tools is capable of comparing multiple groups and/or working with missing values, and only a few allow continuous or multiple covariates. The last of these is of great interest among researchers, as the goal is often to find which regions of the genome are associated with several exposures and traits. To tackle these issues, we have developed an efficient DMC identification method based on Hidden Markov Models (HMMs) called "DMCHMM" which is a three-step approach (model selection, prediction, testing) aiming to address the aforementioned drawbacks.

Depends R (>= 4.1.0), SummarizedExperiment, methods, S4Vectors, BiocParallel, GenomicRanges, IRanges, fdrtool

Imports utils, stats, grDevices, rtracklayer, multcomp, calibrate, graphics

Suggests testthat, knitr, rmarkdown

VignetteBuilder knitr

biocViews DifferentialMethylation, Sequencing, HiddenMarkovModel, Coverage

License GPL-3

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BugReports https://github.com/shokoohi/DMCHMM/issues

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Contents

`DMCHMM-package` *Differentially Methylated CpG using Hidden Markov Model*

Description

DMCHMM is a novel profiling tool for identifying differentially methylated CpG sites using Hidden Markov Model in bisulfite sequencing data.

DMCHMM methods

cBSData, cBSDMCs, methHMEM, methHMMCMC, findDMCs, qqDMCs, manhattanDMCs, readBismark, writeBED.

DMCHMM objects

BSData-class, BSDMCs-class

BSData-class *BSData object*

Description

The BSData object is an S4 class that represents BS-Seq Data.

Arguments

methReads	The matrix methReads contains the number of methylated reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
totalReads	The matrix totalReads contains the number of reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.

Value

A BSData-class object

Slots

methReads An integer matrix

totalReads An integer matrix

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

See Also

SummarizedExperiment objects.

Examples

```
nr <- 500; nc <- 16
metht<-matrix(as.integer(runif(nr * nc, 0, nr)), nr)
methc<-matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep("chr1", nr), IRanges(1:nr, width=1), strand="*")
names(r1) <- 1:nr
cd1<-DataFrame(Group=rep(c("G1","G2"),each=nc/2),row.names=LETTERS[1:nc])
OBJ1<-cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ1
```

BSDMCs-class *BSDMCs object*

Description

The BSDMCs object is an S4 class that represents differentially methylated CpG sites (DMCs) in BS-Seq Data.

Arguments

methReads	The matrix methReads contains the number of methylated reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
totalReads	The matrix totalReads contains the number of reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methLevels	The matrix methLevels contains the predicted methylation level spanning a CpG-site using Hidden Markov model. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methStates	The matrix methStates contains the state of methylation obtained from Hidden Markov model spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData. The value of state is stored in metadata, named Beta.
methVars	The matrix methVars contains the variances of the corresponding methLevels obtianed from MCMC.

Value

A BSDMCs-class object

Slots

methReads An integer matrix

totalReads An integer matrix

methLevels A numeric matrix

methStates An integer matrix

methVars A double matrix

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
nr <- 500; nc <- 16
metht <- matrix(as.integer(runif(nr * nc, 0, nr)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
meths <- matrix(as.integer(runif(nr * nc, 0, 10)), nr)
methl <- methc/metht
methv <- matrix((runif(nr * nc, 0.1, 0.5)), nr)
```

```
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ2 <- cBSDMCs(rowRanges=r1,methReads=methc,totalReads=metht,
methLevels=methl,methStates=meths,methVars=methv,colData=cd1)
OBJ2
```

---

cBSData-method *cBSData method*

Description

Creates a BSData-class object

Usage

```
cBSData(
  methReads,
  totalReads,
  rowRanges,
  colData = DataFrame(row.names = colnames(methReads)),
  metadata = list(),
  ...
)

## S4 method for signature 'matrix,matrix,GRanges'
cBSData(
  methReads,
  totalReads,
  rowRanges,
  colData = DataFrame(row.names = colnames(methReads)),
  metadata = list(),
  ...
)
```

Arguments

methReads	The matrix methReads contains the number of methylated reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
totalReads	The matrix totalReads contains the number of reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
rowRanges	A GRanges or GRangesList object describing the ranges of interest. Names, if present, become the row names of the SummarizedExperiment object. The length of the GRanges or GRangesList must equal the number of rows of the matrices in assays. If rowRanges is missing, a SummarizedExperiment instance is returned.
colData	Object of class "DataFrame" containing information on variable values of the samples
metadata	An optional list of arbitrary content describing the overall experiment
...	other possible parameters

Details

The rows of a BSData object represent ranges (in genomic coordinates) of interest. The ranges of interest are described by a GRanges or a GRangesList object, accessible using the rowRanges function. The GRanges and GRangesList classes contains sequence (e.g., chromosome) name, genomic coordinates, and strand information. Each range can be annotated with additional data; this data might be used to describe the range or to summarize results (e.g., statistics of differential abundance) relevant to the range. Rows may or may not have row names; they often will not.

Value

A BSData-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ1
```

---

cBSDMCs-method *cBSDMCs method*

Description

Creates a BSDMCs-class object

Usage

```
cBSDMCs(
  methReads,
  totalReads,
  methLevels,
  methStates,
  methVars,
  rowRanges,
  colData = DataFrame(row.names = colnames(methReads)),
  metadata = list(),
  ...
)

## S4 method for signature 'matrix,matrix,matrix,matrix,matrix,GRanges'
cBSDMCs(
  methReads,
  totalReads,
```

```
  methLevels,
  methStates,
  methVars,
  rowRanges,
  colData = DataFrame(row.names = colnames(methReads)),
  metadata = list(),
  ...
)
```

Arguments

methReads	The matrix methReads contains the number of methylated reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
totalReads	The matrix totalReads contains the number of reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methLevels	The matrix methLevels contains the predicted methylation level spanning a CpG-site using Hidden Markov model. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methStates	The matrix methStates contains the state of methylation obtained from Hidden Markov model spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData. The value of state is stored in metadata, named Beta.
methVars	The matrix methVars contains the variances of the corresponding methLevels obtianed from MCMC.
rowRanges	A GRanges or GRangesList object describing the ranges of interest. Names, if present, become the row names of the SummarizedExperiment object. The length of the GRanges or GRangesList must equal the number of rows of the matrices in assays. If rowRanges is missing, a SummarizedExperiment instance is returned.
colData	Object of class "DataFrame" containing information on variable values of the samples
metadata	An optional list of arbitrary content describing the overall experiment
...	other possible parameters

Details

The rows of a BSDMCs object represent ranges (in genomic coordinates) of interest. The ranges of interest are described by a GRanges or a GRangesList object, accessible using the rowRanges function. The GRanges and GRangesList classes contains sequence (e.g., chromosome) name, genomic coordinates, and strand information. Each range can be annotated with additional data; this data might be used to describe the range or to summarize results (e.g., statistics of differential abundance) relevant to the range. Rows may or may not have row names; they often will not.

Value

A BSDMCs-class

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
meths <- matrix(as.integer(runif(nr * nc, 0, 10)), nr)
methl <- methc/metht
methv <- matrix((runif(nr * nc, 0.1, 0.5)), nr)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ2 <- cBSDMCs(rowRanges=r1,methReads=methc,totalReads=metht,
methLevels=methl,methStates=meths,methVars=methv,colData=cd1)
OBJ2
```

---

combine-method *combine method*

Description

combine two BSData-class or two BSDMCs-class

Usage

```
combine(obj1, obj2)

## S4 method for signature 'BSData,BSData'
combine(obj1, obj2)

## S4 method for signature 'BSDMCs,BSDMCs'
combine(obj1, obj2)
```

Arguments

obj1	A BSData-class or BSDMCs-class
obj2	A BSData-class or BSDMCs-class

Value

A BSData-class or BSDMCs-class

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc*2, 0, nr)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc*2)),nr,nc*2)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
```

```
cd1 <- DataFrame(Group=rep('G1',each=nc),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc[,1:nc],totalReads=metht[,1:nc],
colData=cd1)
cd2 <- DataFrame(Group=rep('G2',each=nc),row.names=LETTERS[nc+1:nc])
OBJ2 <- cBSData(rowRanges=r1,methReads=methc[,nc+1:nc],totalReads=
metht[,nc+1:nc],colData=cd2)
OBJ3 <- combine(OBJ1, OBJ2)
OBJ3
```

`data` *data*

Description

A part of BS-Seq data for three cell type: WGBS data were derived from whole blood collected on a cohort of healthy individuals from Sweden. Cell lines were separated into T-cells (19 samples), monocytes (13 samples) and B-cells (8 samples). Sequencing was performed on the Illumina HiSeq2000/2500 system for each of the 40 samples, separately. For illustration only 3 samples each containg 30,440 CpG sites around BLK gene are provided here. The whole data are analyzed in the cited paper.

Format

BED files

Details

The data is part of whole blood from Sweeden.

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Source

Genomic Quebec

`findDMCs-method` *findDMCs method*

Description

finds the DMCs after smoothing using HMM

Usage

```
findDMCs(
  object,
  formula,
  FDRthreshold,
  Methylthreshold,
  mc.cores,
  windowsize,
  weightfunction
)

## S4 method for signature 'BSDMCs'
findDMCs(
  object,
  formula,
  FDRthreshold,
  Methylthreshold,
  mc.cores,
  windowsize,
  weightfunction
)
```

Arguments

object	A BSData-class or BSDMCs-class object
formula	A formula
FDRthreshold	A numeric value
Methylthreshold	A positive numeric value; the default is 0.001
mc.cores	An integer greater than 0
windowsize	An integer value for partitioning data into windows of size windowsize.
weightfunction	A function to create weights using variance obtained form the MCMC algorithm

Value

BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ2 <- methHMEM(OBJ1, MaxK=2, mc.cores=2)
```

```
OBJ3 <- methHMMCMC(OBJ2, mc.cores=2)
OBJ4 <- findDMCs(OBJ3, mc.cores=2)
head(metadata(OBJ4)$DMCHMM)
```

---

manhattanDMCs-method *manhattanDMCs method*

Description

Creates a Manhattan plot based on the p-values obtained from `findDMCs` method

Usage

```
manhattanDMCs(
  object,
  col,
  chrlabs,
  suggestiveline,
  genomewideline,
  highlight,
  logp,
  annotatePval,
  annotateTop,
  ...
)

## S4 method for signature 'BSDMCs'
manhattanDMCs(
  object,
  col,
  chrlabs,
  suggestiveline,
  genomewideline,
  highlight,
  logp,
  annotatePval,
  annotateTop,
  ...
)
```

Arguments

`object`	A `BSData-class` or `BSDMCs-class` object
`col`	A character vector indicating which colors to alternate.
`chrlabs`	A character vector equal to the number of chromosomes specifying the chromosome labels (e.g., `c(1:22, "X", "Y", "MT")`).
`suggestiveline`	Where to draw a "suggestive" line. Default -log10(1e-5). Set to FALSE to disable.
`genomewideline`	Where to draw a "genome-wide sigificant" line. Default -log10(5e-8). Set to FALSE to disable.

highlight	A character vector of SNPs in your dataset to highlight. These SNPs should all be in your dataset.
logp	If TRUE, the -log10 of the p-value is plotted. It isn't very useful to plot raw p-values, but plotting the raw value could be useful for other genome-wide plots, for example, peak heights, bayes factors, test statistics, other "scores," etc.
annotatePval	If set, SNPs below this p-value will be annotated on the plot.
annotateTop	If TRUE, only annotates the top hit on each chromosome that is below the annotatePval threshold.
...	other possible parameters

Value

A Manhattan plot

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ2 <- methHMEM(OBJ1, MaxK=2, mc.cores=2)
OBJ3 <- methHMMCMC(OBJ2, mc.cores=2)
OBJ4 <- findDMCs(OBJ3, mc.cores=2)
manhattanDMCs(OBJ4)
```

---

methHMEM-method *methHMEM method*

Description

Estimates the HMM methylation paths and the HMM order for each sample using the EM algorithm

Usage

```
methHMEM(object, MaxK, MaxEmiter, epsEM, useweight, mc.cores)

## S4 method for signature 'BSData'
methHMEM(object, MaxK, MaxEmiter, epsEM, useweight, mc.cores)
```

Arguments

object	A BSData-class or BSDMCs-class object
MaxK	An integer value
MaxEmiter	An integer value
epsEM	A positive numeric value
useweight	A logical value
mc.cores	An integer greater than 0

Value

BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ2 <- methHMEM(OBJ1, MaxK=2, mc.cores=2)
OBJ2
```

---

methHMMCMC-method *methHMMCMC method*

Description

Estimates the HMM methylation paths and the HMM order for each sample using the MCMC algorithm

Usage

```
methHMMCMC(object, useweight, nburn, nthin, nsamp, mc.cores)

## S4 method for signature 'BSDMCs'
methHMMCMC(object, useweight, nburn, nthin, nsamp, mc.cores)
```

Arguments

object	A BSData-class or BSDMCs-class object
useweight	A logical value
nburn	An integer value
nthin	An integer value
nsamp	An integer value
mc.cores	An integer greater than 0

Value

BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ2 <- methHMEM(OBJ1, MaxK=2, mc.cores=2)
OBJ3 <- methHMMCMC(OBJ2, mc.cores=2)
OBJ3
```

---

methLevels-method *methLevels method*

Description

Returns methLevels stored in BSDMCs-class

Assigns methLevels to BSDMCs-class

Usage

```
methLevels(object)

methLevels(object) <- value

## S4 method for signature 'BSDMCs'
methLevels(object)

## S4 replacement method for signature 'BSDMCs,matrix'
methLevels(object) <- value
```

Arguments

object	A BSData-class or BSDMCs-class object
value	An integer matrix

Value

A matrix

A BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
meths <- matrix(as.integer(runif(nr * nc, 0, 10)), nr)
methl <- methc/metht
methv <- matrix((runif(nr * nc, 0.1, 0.5)), nr)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ2 <- cBSDMCs(rowRanges=r1,methReads=methc,totalReads=metht,
methLevels=methl,methStates=meths,methVars=methv,colData=cd1)
methLevels(OBJ2)
methLevels(OBJ2) <- methl
```

---

methReads-method *methReads method*

Description

Returns methReads stored in BSData-class

Assigns methReads to BSData-class

Returns methReads stored in BSDMCs-class

Assigns methReads to BSDMCs-class

Usage

```
methReads(object)

methReads(object) <- value

methReads(object)

methReads(object) <- value

## S4 method for signature 'BSData'
methReads(object)

## S4 replacement method for signature 'BSData,matrix'
methReads(object) <- value

## S4 method for signature 'BSDMCs'
methReads(object)

## S4 replacement method for signature 'BSDMCs,matrix'
methReads(object) <- value
```

Arguments

object	A BSData-class or BSDMCs-class object
value	An integer matrix

Value

A matrix

A BSData-class object

A matrix

A BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
methReads(OBJ1)
methReads(OBJ1) <- methc
```

---

methStates-method *methStates method*

Description

Returns methStates stored in BSDMCs-class

Assigns methStates to BSDMCs-class

Usage

```
methStates(object)

methStates(object) <- value

## S4 method for signature 'BSDMCs'
methStates(object)

## S4 replacement method for signature 'BSDMCs,matrix'
methStates(object) <- value
```

Arguments

object	A BSData-class or BSDMCs-class object
value	An integer matrix

Value

A matrix

A BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
meths <- matrix(as.integer(runif(nr * nc, 0, 10)), nr)
methl <- methc/metht
methv <- matrix((runif(nr * nc, 0.1, 0.5)), nr)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ2 <- cBSDMCs(rowRanges=r1,methReads=methc,totalReads=metht,
methLevels=methl,methStates=meths,methVars=methv,colData=cd1)
methStates(OBJ2)
methStates(OBJ2)<- meths
```

---

methVars-method *methVars method*

Description

Returns methVars stored in BSDMCs-class

Assigns methVars to BSDMCs-class

Usage

```
methVars(object)

methVars(object) <- value

## S4 method for signature 'BSDMCs'
methVars(object)

## S4 replacement method for signature 'BSDMCs,matrix'
methVars(object) <- value
```

Arguments

object	A BSData-class or BSDMCs-class object
value	An integer matrix

Value

A matrix

A BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
meths <- matrix(as.integer(runif(nr * nc, 0, 10)), nr)
methl <- methc/metht
methv <- matrix((runif(nr * nc, 0.1, 0.5)), nr)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ2 <- cBSDMCs(rowRanges=r1,methReads=methc,totalReads=metht,
methLevels=methl,methStates=meths,methVars=methv,colData=cd1)
methVars(OBJ2)
methVars(OBJ2)<- meths
```

---

params *params*

Description

parameters name and their descriptions

Arguments

methReads	The matrix methReads contains the number of methylated reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
totalReads	The matrix totalReads contains the number of reads spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methLevels	The matrix methLevels contains the predicted methylation level spanning a CpG-site using Hidden Markov model. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData.
methVars	The matrix methVars contains the variances of the corresponding methLevels obtianed from MCMC.
methStates	The matrix methStates contains the state of methylation obtained from Hidden Markov model spanning a CpG-site. The rows represent the CpG sites in rowRanges and the columns represent the samples in colData. The value of state is stored in metadata, named Beta.

rowRanges	A GRanges or GRangesList object describing the ranges of interest. Names, if present, become the row names of the SummarizedExperiment object. The length of the GRanges or GRangesList must equal the number of rows of the matrices in assays. If rowRanges is missing, a SummarizedExperiment instance is returned.
colData	Object of class "DataFrame" containing information on variable values of the samples
metadata	An optional list of arbitrary content describing the overall experiment
object	A BSData-class or BSDMCs-class object
value	An integer matrix
obj1	A BSData-class or BSDMCs-class
obj2	A BSData-class or BSDMCs-class
files	A character list
file	A character
name	A character list
MaxK	An integer value
MaxEmiter	An integer value
epsEM	A positive numeric value
useweight	A logical value
mc.cores	An integer greater than 0
nburn	An integer value
nthin	An integer value
nsamp	An integer value
formula	A formula
FDRthreshold	A numeric value
Methylthreshold	A positive numeric value; the default is 0.001
weightfunction	A function to create weights using variance obtained form the MCMC algorithm
...	other possible parameters
col	A character vector indicating which colors to alternate.
chrlabs	A character vector equal to the number of chromosomes specifying the chromosome labels (e.g., c(1:22, "X", "Y", "MT")).
suggestiveline	Where to draw a "suggestive" line. Default -log10(1e-5). Set to FALSE to disable.
genomewideline	Where to draw a "genome-wide sigificant" line. Default -log10(5e-8). Set to FALSE to disable.
highlight	A character vector of SNPs in your dataset to highlight. These SNPs should all be in your dataset.
logp	If TRUE, the -log10 of the p-value is plotted. It isn't very useful to plot raw p-values, but plotting the raw value could be useful for other genome-wide plots, for example, peak heights, bayes factors, test statistics, other "scores," etc.
annotatePval	If set, SNPs below this p-value will be annotated on the plot.
annotateTop	If TRUE, only annotates the top hit on each chromosome that is below the annotatePval threshold.
windowsize	An integer value for partitioning data into windows of size windowsize.

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

---

qqDMCs-method *qqDMCs method*

Description

Creates a Q-Q plot based on the p-values obtained from `findDMCs` method

Usage

```
qqDMCs(object, ...)

## S4 method for signature 'BSDMCs'
qqDMCs(object, ...)
```

Arguments

`object`	A `BSData-class` or `BSDMCs-class` object
`...`	other possible parameters

Value

A QQ plot

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
OBJ2 <- methHMEM(OBJ1, MaxK=2, mc.cores=2)
OBJ3 <- methHMMCMC(OBJ2, mc.cores=2)
OBJ4 <- findDMCs(OBJ3, mc.cores=2)
qqDMCs(OBJ4)
```

readBismark-method *readBismark method*

Description

reads BS-Seq data

Usage

```
readBismark(files, colData, mc.cores)

## S4 method for signature 'character,DataFrame,numeric'
readBismark(files, colData, mc.cores)

## S4 method for signature 'character,data.frame,numeric'
readBismark(files, colData, mc.cores)

## S4 method for signature 'character,character,numeric'
readBismark(files, colData, mc.cores)
```

Arguments

files	A character list
colData	Object of class "DataFrame" containing information on variable values of the samples
mc.cores	An integer greater than 0

Value

A BSData-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
fn <- list.files(system.file('extdata',package = 'DMCHMM'))
fn.f <- list.files(system.file('extdata',package='DMCHMM'), full.names=TRUE)
OBJ <- readBismark(fn.f, fn, mc.cores=2)
cdOBJ <- DataFrame(Cell = factor(c('BC', 'TC','Mono'),
labels = c('BC', 'TC', 'Mono')), row.names = c('BCU1568','BCU173','BCU551'))
colData(OBJ) <- cdOBJ
OBJ
```

totalReads-method *totalReads method*

Description

Returns totalReads stored in BSData-class

Assigns totalReads to BSData-class

Returns totalReads stored in BSDMCs-class

Assigns totalReads to BSDMCs-class

Usage

```
totalReads(object)

totalReads(object) <- value

totalReads(object)

totalReads(object) <- value

## S4 method for signature 'BSData'
totalReads(object)

## S4 replacement method for signature 'BSData,matrix'
totalReads(object) <- value

## S4 method for signature 'BSDMCs'
totalReads(object)

## S4 replacement method for signature 'BSDMCs,matrix'
totalReads(object) <- value
```

Arguments

object	A BSData-class or BSDMCs-class object
value	An integer matrix

Value

A matrix

A BSData-class object

A matrix

A BSDMCs-class object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
nr <- 150; nc <- 8
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n=nr*nc,c(metht),prob = runif(nr*nc)),nr,nc)
r1 <- GRanges(rep('chr1', nr), IRanges(1:nr, width=1), strand='*')
names(r1) <- 1:nr
cd1 <- DataFrame(Group=rep(c('G1','G2'),each=nc/2),row.names=LETTERS[1:nc])
OBJ1 <- cBSData(rowRanges=r1,methReads=methc,totalReads=metht,colData=cd1)
totalReads(OBJ1)
totalReads(OBJ1) <- metht
```

`writeBED-method` *writeBED method*

Description

write BS-Seq data to BED files

Usage

```
writeBED(object, name, file)

## S4 method for signature 'BSData,character,character'
writeBED(object, name, file)

## S4 method for signature 'BSData,character,missing'
writeBED(object, name)

## S4 method for signature 'BSData,missing,character'
writeBED(object, file)

## S4 method for signature 'BSData,missing,missing'
writeBED(object)

## S4 method for signature 'BSDMCs,character,character'
writeBED(object, name, file)

## S4 method for signature 'BSDMCs,character,missing'
writeBED(object, name)

## S4 method for signature 'BSDMCs,missing,character'
writeBED(object, file)

## S4 method for signature 'BSDMCs,missing,missing'
writeBED(object)
```

Arguments

`object`	A `BSData-class` or `BSDMCs-class` object
`name`	A character list
`file`	A character

Value

BED files

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Index