

Package ‘DMCFB’

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Type Package

Title Differentially Methylated Cytosines via a Bayesian Functional Approach

Version 1.18.0

Description DMCFB is a pipeline for identifying differentially methylated cytosines using a Bayesian functional regression model in bisulfite sequencing data. By using a functional regression data model, it tries to capture position-specific, group-specific and other covariates-specific methylation patterns as well as spatial correlation patterns and unknown underlying models of methylation data. It is robust and flexible with respect to the true underlying models and inclusion of any covariates, and the missing values are imputed using spatial correlation between positions and samples. A Bayesian approach is adopted for estimation and inference in the proposed method.

Depends R (>= 4.0.0), SummarizedExperiment, methods, S4Vectors, BiocParallel, GenomicRanges, IRanges

Imports utils, stats, speedglm, MASS, data.table, splines, arm, rtracklayer, benchmarkme, tibble, matrixStats, fastDummies, graphics

Suggests testthat, knitr, rmarkdown, BiocStyle

VignetteBuilder knitr

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License GPL-3

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| | |
|---------------|--|
| DMCFB-package | <i>Differentially Methylated cytosines using functional Bayesian regression models</i> |
|---------------|--|

Description

DMCFB is a profiling tool for identifying differentially methylated cytosines using Functional Bayesian Model in bisulfite sequencing data.

DMCFB methods

[findDMCFB](#), [plotDMCFB](#), [cBSDMC](#), [readBismark](#).

BSDMC objects

[BSDMC-class](#)

BSDMC-class

BSDMC object

Description

The BSDMC 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 Bayesian functional regression models. The rows represent the CpG sites in `rowRanges` and the columns represent the samples in `colData`.

Value

A [BSDMC-class](#) object

Slots

`methReads` An integer matrix
`totalReads` An integer matrix
`methLevels` A numeric matrix

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

See Also

[RangedSummarizedExperiment-class](#) [GRanges-class](#)

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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, methStates = meths, methVars = methv, colData = cd1
)
OBJ2

```

cBSDMC-method

cBSDMC method

Description

Creates a [BSDMC-class](#) object

Usage

```

cBSDMC(
  methReads,
  totalReads,
  methLevels,
  rowRanges,
  colData = DataFrame(row.names = colnames(methReads)),
  metadata = list(),
  ...
)

## S4 method for signature 'matrix,matrix,matrix,GRanges'
cBSDMC(
  methReads,
  totalReads,
  methLevels,
  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 Bayesian functional regression models. 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 | A list of storing MCMC samples or DMCs |
| ... | other possible parameters |

Details

The rows of a BSDMC 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 BSDMC-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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, methStates = meths, methVars = methv, colData = cd1
)
```

OBJ2

| | |
|----------------|-----------------------|
| combine-method | <i>combine method</i> |
|----------------|-----------------------|

Description

combine two [BSDMC-class](#) or two [BSDMC-class](#)

Usage

```
combine(obj1, obj2)

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

Arguments

| | |
|------|-------------------------------|
| obj1 | A BSDMC-class |
| obj2 | A BSDMC-class |

Value

A [BSDMC-class](#) or [BSDMC-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
)
methl <- methc / metht
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 <- cBSDMC(
  rowRanges = r1, methReads = methc[, 1:nc], totalReads = metht[, 1:nc],
  methLevels = methl[, 1:nc], colData = cd1
)
cd2 <- DataFrame(
  Group = rep("G2", each = nc),
```

```
    row.names = LETTERS[nc + 1:nc]
  )
  OBJ2 <- cBSDMC(
    rowRanges = r1, methReads = methc[, nc + 1:nc], totalReads =
      metht[, nc + 1:nc], methLevels = methl[, nc + 1:nc], colData = cd2
  )
  OBJ3 <- combine(OBJ1, OBJ2)
  OBJ3
```

| | |
|------------------|-------------------------|
| findDMCFB-method | <i>findDMCFB method</i> |
|------------------|-------------------------|

Description

DMC identification via Bayesian functional regression models

Usage

```
findDMCFB(
  object,
  bwa,
  bwb,
  nBurn,
  nMC,
  nThin,
  alpha,
  sdv,
  nCores,
  pSize,
  sfiles
)

## S4 method for signature 'BSDMC'
findDMCFB(
  object,
  bwa,
  bwb,
  nBurn,
  nMC,
  nThin,
  alpha,
  sdv,
  nCores,
  pSize,
  sfiles
)
```

Arguments

| | |
|--------|---|
| object | A BSDMC-class object |
| bwa | An integer value specifying the band-width size of B-spline basis matrix for a natural cubic spline for the group-specific effects of the Bayesian functional regression model |
| bwb | An integer value specifying the band-width size of B-spline basis matrix for a natural cubic spline for the individual-specific effects of the Bayesian functional regression model |
| nBurn | An integer value specifying the number of burn-in samples |
| nMC | An integer value specifying the number of MCMC samples after burn-in |
| nThin | An integer value specifying the thinning number in MCMC |
| alpha | A numeric value specifying the level of α in credible interval $(1 - \alpha)\%$ |
| sdv | An double value specifying the standard deviation of priors |
| nCores | An integer value specifying the number of machine cores for parallel computing |
| pSize | An integer value specifying the number of cytosines in a region to be used in a Bayesian functional regression model for DMC detection |
| sfiles | A logical value indicating whether files to be saved or not. |

Value

[BSDMC-class](#) object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```

set.seed(1980)
nr <- 1000
nc <- 4
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n = nr * nc, c(metht), prob = runif(nr * nc)), nr, nc)
methl <- methc / metht
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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, colData = cd1
)
OBJ2 <- findDMCFB(OBJ1,
  bwa = 10, bwb = 10, nBurn = 50, nMC = 50, nThin = 1,
  alpha = 0.05, nCores = 2, pSize = 500, sfiles = FALSE

```



```
)  
OBJ2
```

| | |
|-------------------|--------------------------|
| methLevels-method | <i>methLevels method</i> |
|-------------------|--------------------------|

Description

Returns methLevels stored in [BSDMC-class](#)

Assigns methLevels to [BSDMC-class](#)

Usage

```
methLevels(object)
```

```
methLevels(object) <- value
```

```
## S4 method for signature 'BSDMC'
```

```
methLevels(object)
```

```
## S4 replacement method for signature 'BSDMC,matrix'
```

```
methLevels(object) <- value
```

Arguments

object A [BSDMC-class](#) object

value An integer matrix

Value

A matrix

A [BSDMC-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)  
methl <- methc / metht  
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 <- cBSDMC(
    rowRanges = r1, methReads = methc, totalReads = metht,
    methLevels = methl, colData = cd1
  )
  methLevels(OBJ1)
  methLevels(OBJ1) <- methl
```

methReads-method *methReads method*

Description

Returns methReads stored in [BSDMC-class](#)

Assigns methReads to [BSDMC-class](#)

Usage

```
methReads(object)
```

```
methReads(object) <- value
```

```
## S4 method for signature 'BSDMC'
```

```
methReads(object)
```

```
## S4 replacement method for signature 'BSDMC,matrix'
```

```
methReads(object) <- value
```

Arguments

object A [BSDMC-class](#) object

value An integer matrix

Value

A matrix

A [BSDMC-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)
methl <- methc / metht
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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, colData = cd1
)
methReads(OBJ1)
methReads(OBJ1) <- methc

```

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 Bayesian functional regression models. 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 | A list of storing MCMC samples or DMCs |
| object | A BSDMC-class object |

| | |
|----------|---|
| value | An integer matrix |
| name | A character list |
| obj1 | A BSDMC-class |
| obj2 | A BSDMC-class |
| files | A character list |
| file | A character |
| nCores | An integer value specifying the number of machine cores for parallel computing |
| mc.cores | An integer greater than 0 |
| pSize | An integer value specifying the number of cytosines in a region to be used in a Bayesian functional regression model for DMC detection |
| bwa | An integer value specifying the band-width size of B-spline basis matrix for a natural cubic spline for the group-specific effects of the Bayesian functional regression model |
| bwb | An integer value specifying the band-width size of B-spline basis matrix for a natural cubic spline for the individual-specific effects of the Bayesian functional regression model |
| nBurn | An integer value specifying the number of burn-in samples |
| nThin | An integer value specifying the thinning number in MCMC |
| nMC | An integer value specifying the number of MCMC samples after burn-in |
| sdv | An double value specifying the standard deviation of priors |
| alpha | A numeric value specifying the level of α in credible interval $(1 - \alpha)\%$ |
| col | A character vector indicating which colors to alternate. |
| sfiles | A logical value indicating whether files to be saved or not. |
| region | An integer vector of length two specifying which subset of the object to be plotted |
| nSplit | A integer value specifying the number of subsets must be done for plotting the results of DMC identification |
| parList | A list specifying plots parameters, see par |
| ... | other possible parameters |

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

| | |
|------------------|-------------------------|
| plotDMCFB-method | <i>plotDMCFB method</i> |
|------------------|-------------------------|

Description

Plotting the results of DMC identification stored in a [BSDMC-class](#) object

Usage

```
plotDMCFB(object, region, nSplit, parList)
```

```
## S4 method for signature 'BSDMC'
```

```
plotDMCFB(object, region, nSplit, parList)
```

Arguments

| | |
|---------|--|
| object | A BSDMC-class object |
| region | An integer vector of length two specifying which subset of the object to be plotted |
| nSplit | A integer value specifying the number of subsets must be done for plotting the results of DMC identification |
| parList | A list specifying plots parameters, see par |

Value

Plot

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
set.seed(1980)
nr <- 1000
nc <- 4
metht <- matrix(as.integer(runif(nr * nc, 0, 100)), nr)
methc <- matrix(rbinom(n = nr * nc, c(metht), prob = runif(nr * nc)), nr, nc)
methl <- methc / metht
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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, colData = cd1
```

```
)  
OBJ2 <- findDMCFB(OBJ1,  
  bwa = 10, bwb = 10, nBurn = 50, nMC = 50, nThin = 1,  
  alpha = 0.05, nCores = 2, pSize = 500, sfiles = FALSE  
)  
plotDMCFB(OBJ2)
```

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 [BSDMC-class](#) object

Author(s)

Farhad Shokoohi <shokoohi@icloud.com>

Examples

```
fn <- list.files(system.file("extdata", package = "DMCFB"))
fn.f <- list.files(system.file("extdata", package = "DMCFB"),
  full.names = TRUE
)
OBJ <- readBismark(fn.f, fn, mc.cores=1)
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 | <i>totalReads method</i> |
|-------------------|--------------------------|

Description

Returns totalReads stored in [BSDMC-class](#)

Assigns totalReads to [BSDMC-class](#)

Usage

```
totalReads(object)
```

```
totalReads(object) <- value
```

```
## S4 method for signature 'BSDMC'
```

```
totalReads(object)
```

```
## S4 replacement method for signature 'BSDMC,matrix'
```

```
totalReads(object) <- value
```

Arguments

object A [BSDMC-class](#) object

value An integer matrix

Value

A matrix

A [BSDMC-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)
methl <- methc / metht
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 <- cBSDMC(
  rowRanges = r1, methReads = methc, totalReads = metht,
  methLevels = methl, colData = cd1
)
totalReads(OBJ1)
totalReads(OBJ1) <- metht
```


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