Package 'SIMD'

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Type Package

Title Statistical Inferences with MeDIP-seq Data (SIMD) to infer the methylation level for each CpG site

Version 1.25.0

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Description This package provides a inferential analysis method for detecting differentially expressed CpG sites in MeDIP-seq data. It uses statistical framework and EM algorithm, to identify differentially expressed CpG sites. The methods on this package are described in the article 'Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data' by Yan Zhou, Jiadi Zhu, Mingtao Zhao, Baoxue Zhang, Chunfu Jiang and Xiyan Yang (2018, pending publication).

License GPL-3

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Contents

`SIMD-package` *A method to infer the methylation expression level for each CpG sites.*

Description

SIMD is a package to infer the methylation expression level for each CpG sites.The main idea of SIMD is that by using statistical inference to with Medip-seq data method to infer the methylation level.

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References

Zhou Y. (2018). Methylation-level inferences and detection of differential methylation with Medip-seq data.

all_CpGsite_bin_chr18 *A simulation dataset of CpG sites.*

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the CpG sites.

Usage

```
all_CpGsite_bin_chr18
```

Format

A data.frame containing 2000 CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

classifypvalue *calculate P-value in code EMtest.*

Description

calculate P-value in code EMtest.

Usage

```
classifypvalue(type1, type2, type3, type4, sm1chring1, sm1chring2, sm1chring3,
  sm1chring4, p, typelength, sm1chringlength, pvalue = rep(0,
  length(sm1chring1)))
```

Arguments

type1	The first colum of the first matrix.
type2	The second colum of the first matrix.
type3	The third colum of the first matrix.
type4	The fourth colum of the first matrix.
sm1chring1	The first colum of the second matrix.
sm1chring2	The second colum of the second matrix.
sm1chring3	The third colum of the second matrix.
sm1chring4	The forth colum of the second matrix.
p	P-value.
typelength	The nrows of the first matrix.
sm1chringlength	The nrows of the second matrix.
pvalue	A vector, the length equals to the nrows of the second matrix.

Value

The probability.

EM2_H1ESB1_MeDIP_sigleCpG

A simulation dataset of MeDIP CpG sites.

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MeDIP CpG sites.

Usage

```
EM2_H1ESB1_MeDIP_sigleCpG
```

Format

A data.frame containing 2000 MeDIP CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

EM2_H1ESB2_MeDIP_sigleCpG

A simulation dataset of MeDIP CpG sites.

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MeDIP CpG sites.

Usage

```
EM2_H1ESB2_MeDIP_sigleCpG
```

Format

A data.frame containing 2000 MeDIP CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

EMalgorithm

EM algorithm to infer CpG sites.

Description

Using EM algorithm to infer the real number of CpG sites.

Usage

```
EMalgorithm(cpgsitefile, allcpgfile, category = "1", writefile = NULL,
  reportfile = NULL)
```

Arguments

cpgsitefile	The path of file to store CpG site.
allcpgfile	The file to store CpG sites.
category	Default to "1".
writefile	The path of output results. (If writefile=NULL, there will return the results back to main program.)
reportfile	The path of output results.

Value

values or file If writefile is NULL, then return the values of results,otherwise output to write file.

Examples

```
datafile <- system.file("extdata", package="methylMnM")
data(example_data)
filepath <- datafile[1]
allcpgfile <- EM_H1ESB1_MeDIP_sigleCpG
dirwrite <- paste(setwd(getwd()), "/", sep="")
readshort <- paste(filepath, "/H1ESB1_MeDIP_18.extended.txt", sep="")
writefile <- paste(dirwrite, "EM2_H1ESB1_MeDIP_sigleCpG.bed", sep="")
reportfile <- paste(dirwrite, "EM2_H1ESB1_MeDIP_sigleCpG_report.bed", sep="")
f <- EMalgorithm(cpgsitefile=readshort, allcpgfile=allcpgfile, category="1",
                 writefile=writefile, reportfile=reportfile)
```

---

emalgth *Calculate the probability on condition that the sums equal to 1.*

Description

Calculate the probability on condition that only a single CpG contributes to a short read.

Usage

```
emalgth(X)
```

Arguments

X	A matrix about X, the elements in X takes values on 0,1 and satisfy the sums of each row equal to 1.

Value

y1 The probability when sums equal to 1.

Examples

```
set.seed(123)
d <- matrix(0, nrow=200, ncol=50)
random_num <- sample(1:50, 200, replace=TRUE)
for(i in 1:nrow(d)){
    d[i,random_num[i]]<-1
}
result <- emalgth(d)
head(result)
```

emalgth1 *Calculate the probability on condition that the sums more than 1.*

Description

Calculate the probability on condition that at least a CpG contributes to a short read.

Usage

```
emalgth1(X)
```

Arguments

X	A matrix about X, the elements in X takes values on 0,1 and satisfy the sums of each row more than 1.

Value

y1 The probability when sums more than 1.

Examples

```
set.seed(123)
d <- matrix(0, nrow=200, ncol=50)
random_num <- sample(1:10, 200, replace=TRUE)
for(i in 1:nrow(d)){
    temp <- sample(1:50, random_num[i], replace=FALSE)
    d[i,temp] <- 1
}
result <- emalgth1(d)
head(result)
```

EMtest *Inferring the methylation expression level of single sites.*

Description

Using statistical framework and EM algorithm to infer the methylation expression level of single sites.

Usage

```
EMtest(datafile = NULL, chrstring = NULL, cpgfile, mrecpgfile = NULL,
  writefile = NULL, reportfile = NULL, mreratio = 3/7, psd = 2,
  mkadded = 1, f = 1)
```

Arguments

datafile	The files of sample. (datafile should be cbind(data1,data2, data3,data4), where data1 and data2 are Medip-seq data, data3 and data4 are MRE-seq data).
chrstring	The chromosome should be test.
cpgfile	The file of all CpG number.
mrecpgfile	The file of MRE-CpG number(If NULL, mrecpgfile will equal to cpgfile).
writefile	The path of file of output result. (If writefile=NULL, there will return the results back to main program)
reportfile	The path of output results of the number of bin, total reads before processing and total reads after processing.
mreratio	The ratio of total unmethylation level with total methylation level (Defaulted mreratio is 3/7).
psd	The parameters of pseudo count, which pseudo count added to Medip-seq and MRE-seq count.
mkadded	Added to all CpG and MRE CpG (We set psd=2 and mkadded=1 as defaulted for robust).
f	Adjustment weight, default to 1.

Value

values or file The output file "writefile" will own eleven columns, that is, "chr", "chrSt", "chrEnd", "Medip1", "Medip2", "MRE1", "MRE2", "cg","mrecg","pvalue" and "Ts". We also output a report file which will include parameters "s1/s2", "s3/s4", "N1", "N2", "N3", "N4", "c1", "c2", "Number of windows" and "Spend time".

Examples

```
data(example_data)
data1 <- EM2_H1ESB1_MeDIP_sigleCpG
data2 <- EM2_H1ESB2_MeDIP_sigleCpG
data3 <- H1ESB1_MRE_sigleCpG
data4 <- H1ESB2_MRE_sigleCpG
datafile <- cbind(data1, data2, data3, data4)
allcpg <- all_CpGsite_bin_chr18
mrecpg <- three_mre_cpg
dirwrite <- paste(setwd(getwd()), "/", sep="")
writefile <- paste(dirwrite, "pval_EM_H1ESB1_H1ESB21.bed", sep="")
reportfile <- paste(dirwrite, "report_pvalH1ESB1_H1ESB21.bed", sep="")
EMtest(datafile=datafile, chrstring=NULL, cpgfile=allcpg,
       mrecpgfile=mrecpg, writefile=writefile, reportfile=reportfile,
       mreratio=3/7, psd=2, mkadded=1, f=1)
```

EM_H1ESB1_MeDIP_sigleCpG

A simulation dataset of MeDIP CpG sites.

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MeDIP CpG sites.

Usage

```
EM_H1ESB1_MeDIP_sigleCpG
```

Format

A data.frame containing 2000 MeDIP CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

H1ESB1_MRE_sigleCpG *A simulation dataset of MRE CpG sites.*

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MRE CpG sites.

Usage

```
H1ESB1_MRE_sigleCpG
```

Format

A data.frame containing 2000 MRE CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

`H1ESB2_MRE_sigleCpG` *A simulation dataset of MRE CpG sites.*

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MRE CpG sites.

Usage

```
H1ESB2_MRE_sigleCpG
```

Format

A data.frame containing 2000 MRE CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

probBinom *Compute P-values for Medip-seq and MRE-seq data.*

Description

Compute P-values.

Usage

```
probBinom(t, size1, size2, c1, c2)
```

Arguments

t	The real value for random variable according to dataset.
size1	The sum of Medip-seq real reads of the each CpG site for control and treatment sample.
size2	The sum of MRE-seq real reads of the each CpG site for control and treatment sample.
c1	The scaling factor for MeDip-seq data.
c2	The scaling factor for MRE-seq data.

Value

p The P-values for testing the methylation expression levels for each CpG sites.

Examples

```
set.seed(1234)
t <- 0.1
size1 <- sample(1:1000, 1, replace=TRUE)
size2 <- sample(1:1000, 1, replace=TRUE)
c1 <- 1
c2 <- 2
result <- probBinom(t, size1, size2, c1, c2)
```

three_mre_cpg *A simulation dataset of MRE CpG sites.*

Description

This data set gives 2000 CpG sites which include the chromosome of the region, the start and the stop position of the MRE CpG sites.

Usage

```
three_mre_cpg
```

Format

A data.frame containing 2000 MRE CpG sites.

Source

Zhang, B., Zhou, Y., et al. (2013). Functional DNA methylation differences between tissues, cell types, and across individuals discovered using the M&M algorithm. Genome Research. 23: 1522-1540.

References

Zhou Y. (2018). Methylation-level Inferences and Detection of Differential Methylation with Medip-seq Data.

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