Package 'MEDME'

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Type Package

Title Modelling Experimental Data from MeDIP Enrichment

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Description MEDME allows the prediction of absolute and relative methylation levels based on measures obtained by MeDIP-microarray experiments

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Imports Biostrings, MASS, drc

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CGcount *Determining the count of CpG dinucleotides for a set of genomic locations*

Description

The count of CpGs is determined in each window of size wsize, with or withouth weighting, for each probe according to its position, chromosome and genome realease

Usage

```
CGcount(data, wsize = 1000, wFunction = "linear")
```

Arguments

data	An object of class MEDMEset
wsize	number; the size of the smoothing window, in bp
wFunction	string; the type of weighting function, to choose among linear, exp, log or none

Details

Only human and mouse are currently supported. The respective genomic sequence metadata library needs to be downloaded from the Bioconductor website, installed and loaded (around 800Mb). Please note that only the last genome release should be used. LiftOver UCSC tool could be used for batch conversion of old genomic position to the last genome release.

Value

An object of class MEDMEset is returned where the count of CpGs for each probe has been saved on the CGcount slot.

See Also

smooth

Examples

```
data(testMEDMEset)
## just an example with the first 1000 probes
testMEDMEset = smooth(data = testMEDMEset[1:1000,])
library(BSgenome.Hsapiens.UCSC.hg18)
testMEDMEset = CGcount(data = testMEDMEset)
```

MEDME *Determining the logistic model of MeDIP enrichment in respect to the expected DNA methylation level*

Description

Probe-level MeDIP weighted enrichment is compared to the expected DNA methytlation level. The former is determined applying MeDIP protocol to a fully methylated DNA. The latter is determined as the count of CpGs for each probe. This is assumed to be the methylation level of each probe in a fully methylated sample.

Usage

```
MEDME(data, sample, CGcountThr = 1, figName = NULL)
```

Arguments

data	An object of class MEDMEset
sample	Integer; the number of the sample to be used to fit the model, based on the order of samples in the smoothed slot
CGcountThr	number; the threshold to avoid modelling probes with really low methylation level, i.e. CpG count
figName	string; the name of the file reporting the model fitting

Details

The model should be applied on calibration data containing MeDIP enrichment of fully methylated DNA, most likely artificially generated (see references). Nevertheless, in case chromosome or genome-wide human tiling arrays are used a regular sample could be used too. In fact, human genomic DNA is known to be hyper-methylated but in the promoter regions. Of course the performance of the method is expected to be somehow affected by this approximation.

Value

The logistic model as returned from the multdrc function from the drc R library

References

http://genome.cshlp.org/cgi/content/abstract/gr.080721.108v1

See Also

smooth, CGcount

Examples

```
data(testMEDMEset)
## just an example with the first 1000 probes
testMEDMEset = smooth(data = testMEDMEset[1:1000, ])
library(BSgenome.Hsapiens.UCSC.hg18)
testMEDMEset = CGcount(data = testMEDMEset)
MEDMEmodel = MEDME(data = testMEDMEset, sample = 1, CGcountThr = 1, figName = NULL)
```

MEDME.predict *Applying the logistic model on MeDIP enrichment data*

Description

This allows the probe-level determination of MeDIP smoothed data, as well as absolute and relative methylation levels (AMS and RMS respectively)

Usage

```
MEDME.predict(data, MEDMEfit, MEDMEextremes = c(1,32), wsize = 1000, wFunction='linear')
```

Arguments

data	An object of class MEDMEset
MEDMEfit	the model obtained from the MEDME.model function
MEDMEextremes	vector; the background and saturation values as determined by the fitting of the model on the calibration data
wsize	number; the size of the smoothing window, in bp
wFunction	string; the type of weighting function, to choose among linear, exp, log or none

Value

An object of class MEDMEset. The resulting smoothed data, the absolute and relative methylation score (AMS and RMS) are saved in the smoothed, AMS and RMS slots, respectively.

References

http://genome.cshlp.org/cgi/content/abstract/gr.080721.108v1

See Also

smooth, CGcount, MEDME

Examples

```
data(testMEDMEset)
## just an example with the first 1000 probes
testMEDMEset = smooth(data = testMEDMEset[1:1000, ])
library(BSgenome.Hsapiens.UCSC.hg18)
testMEDMEset = CGcount(data = testMEDMEset)
MEDMEmodel = MEDME(data = testMEDMEset, sample = 1, CGcountThr = 1, figName = NULL)
testMEDMEset = MEDME.predict(data = testMEDMEset, MEDMEfit = MEDMEmodel, MEDMEextremes = c(1,32), wsize = 1000,
```

MEDME.readFiles *reading sgr or gff files for MEDME*

Description

allows to read sgr or gff files before submitting the data to MEDME analysis

Usage

```
MEDME.readFiles(path = getwd(), files = NULL, format, organism)
```

Arguments

path	string; the path where the files are stored; the current working directory is the default
files	vector; optional vector of file names
format	string; either sgr or gff to indicate the respective file formats
organism	string; either hsa or mmu for homo sapiens and mus musculus respectively

Details

In case of GFF files (recommendend), tab-delimited files with header are expected with following fields: chromosome, probe ids, start and stop chromosomal positions, and score are expected in columns 1, 3, 4, 5 and 6 repectively. Multiple files are also expected to be in the same order of rows.

In case of sgr files (GFF is the preferred format), tab-delimited files with no header and chr, chr positions and score are expected in columns 1, 2 and 3 repectively. Multiple files are also expected to be in the same order of rows.

Value

An object of class MEDMEset. The column headers in the logR slot are determined from the file names. in case of SGR files the are not probe names and progressive numbers are used in place of them. In case of GFF files the probe names are determined from the 3rd column.

MEDME.writeFiles *writeFiles sgr or gff files from MEDME output*

Description

allows to write sgr or gff files after MEDME analysis

Usage

```
MEDME.writeFiles(data, output, path = getwd(), format, featureLength  = NULL)
```

Arguments

data	An object of class MEDMEset
output	string; the name of the data slot to be written on the disk, either logR, smoothed, AMS or RMS
path	string; the path where the files are stored; the current working directory is the default
format	string; either sgr or gff to indicate the respective file formats
featureLength	integer; in case of GFF file format the length of the features has to be provided to determine start and end positions

Details

One GFF or SGR file is provided for each sample of the data MEDMEset object.

In case of GFF files, tab-delimited files with header are provided with following fields for each probe: chromosome, empty field, probe ids, start and stop chromosomal positions, and score and empty fields.

In case of sgr files, tab-delimited files with no header and chr, chr positions and score are provided.

MEDMEset-class *Class "MEDMEset"*

Description

This class is used in MEDME library to store MeDIP derived DNA-methylation estimates and to save further elaboration of these, in association with chromosomal and positional probe information

Objects from the Class

Objects can be created by calls of the form `new("MEDMEset", ...)`. This object could initially host the MeDIP normalized logRatio data, as returned by the `MEDME.readFiles` function. Afterwards, the same obejct is returned by most of the MEDME library function. Each time, a new slot is filled with additional data, as smoothed logR or Absolute/Relative Methylation Scores (AMS and RMS respectively). At the end of the analysis, usually after a call to the `MEDME.predict` function, the `MEDME.writeFiles` function can be used to generate SGR or GFF files from this object.

Slots

chr: Object of class `"character"` : the probe-level chromosome asignments

pos: Object of class `"numeric"` : the probe-level genomic position

logR: Object of class `"matrix"` : the probe-level un-trasformed normalized MeDIP logRatios for each sample

smoothed: Object of class `"matrix"` : the probe-level smoothed MeDIP logRatios for each sample

AMS: Object of class `"matrix"` : the probe-level Absolute Methylation Score for each sample

RMS: Object of class `"matrix"` : the probe-level Relative Methylation Score for each sample

CGcounts: Object of class `"numeric"` : the probe-level count of CpGs

organism: Object of class `"character"` : the organism that the probe genomic positions are referring to, either hsa or mmu for homo sapiens or mus musculus respectively

Methods

[`signature(x = "MEDMEset")`: subsets the object based on its probes and/or samples

AMS `signature(object = "MEDMEset")`: extracts the Absolute Methylation Score from the AMS slot

CG `signature(object = "MEDMEset")`: extracts the probe CpG count from the CGcounts slot

chr `signature(object = "MEDMEset")`: extracts the probe chromosomal assignment

org `signature(object = "MEDMEset")`: extracts the organism

initialize `signature(.Object = "MEDMEset")`: automatically generates smoothed, AMS and RMS matrix when only the logR slot is filled

logR `signature(object = "MEDMEset")`: extracts the matrix of MeDIP un-transformed logRatios

pos `signature(object = "MEDMEset")`: extracts the probe genomic position

RMS `signature(object = "MEDMEset")`: extracts the Relative Methylation Score from the RMS slot

show `signature(object = "MEDMEset")`: prints a summary of the object content

smoothed `signature(object = "MEDMEset")`: extracts the Absolute Methylation Score from the AMS slot

Author(s)

Mattia Pelizzola

References

http://genome.cshlp.org/cgi/content/abstract/gr.080721.108v1

See Also

MEDME.readFiles, MEDME.writeFiles

Examples

```
showClass("MEDMEset")
```

---

smooth *Determining weighted MeDIP data*

Description

MeDIP data from tiling arrays are smoothed by determining for each probe i the weighted average of the probes within a window of size wsize centered at i

Usage

```
smooth(data, wsize=1000, wFunction='linear')
```

Arguments

`data`	An object of class MEDMEset
`wsize`	number; the size of the smoothing window, in bp
`wFunction`	string; the type of weighting function, to choose among linear, exp, log or none

Details

The un-smoothed data are read from the slot logR of the data MEDMEset and the resulting smoothed data are saved on the smoothed slot.

Value

An object of class MEDMEset. In particular, the smoothed data are saved on the smoothed slot.

Examples

```
data(testMEDMEset)
# just an example with the first 1000 probes
testMEDMEset = smooth(data = testMEDMEset[1:1000,])
```

---

testMEDMEset *Dataset of class MEDMEset for testing MEDME*

Description

This dataset contains a subset of the data reported in references. It contains normalized un-smoothed probe-level MeDIP enrichment for almost 50000 probes. This is a random subset of a custom Nimblegen chromosome X tiling array. It is a two channels array with an resolution of 100bp and oligos of 60nt. The M value is reported only. The fullyMet column of the logR slot contains data from a calibration experiments where MeDIP has been applied to a fully methylated sample. The last two columns NBMEL and YUSAC2 contain DNA-methylation experimental data for two cell strains: NBMEL are newborn normal melanocytes cells and YUSAC2 a melanoma strain. Data was processed with within and between array normalization. The full dataset contains almost 380K probes. See references for details. Chromosome, genomic position and logR of probes can be accessed with the methods chr, pos and logR respectively.

Please note that the original genomic coordinates were mapped to the hg17 human genome. These have been converted to hg18 using the LiftOver USCS tool available online for batch conversion.

Usage

```
data(testMEDMEset)
```

Format

MEDMEset

References

http://genome.cshlp.org/cgi/content/abstract/gr.080721.108v1

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