# Package 'MEDIPS'

## September 16, 2024

Type Package Title DNA IP-seq data analysis **Version** 1.56.0 Date 2020-02-15 Author Lukas Chavez, Matthias Lienhard, Joern Dietrich, Isaac Lopez Moyado Maintainer Lukas Chavez < lukas chavez@ucsd.edu> **Description** MEDIPS was developed for analyzing data derived from methylated DNA immunoprecipitation (MeDIP) experiments followed by sequencing (MeDIPseq). However, MEDIPS provides functionalities for the analysis of any kind of quantitative sequencing data (e.g. ChIP-seq, MBD-seq, CMS-seq and others) including calculation of differential coverage between groups of samples and saturation and correlation analysis. License GPL (>=2) LazyLoad yes **Depends** R (>= 3.0), BSgenome, Rsamtools Imports GenomicRanges, Biostrings, graphics, gtools, IRanges, methods, stats, utils, edgeR, DNAcopy, biomaRt, rtracklayer, preprocessCore Suggests BSgenome. Hsapiens. UCSC. hg19, MEDIPSData, BiocStyle biocViews DNAMethylation, CpGIsland, DifferentialExpression, Sequencing, ChIPSeq, Preprocessing, QualityControl, Visualization, Microarray, Genetics, Coverage, GenomeAnnotation, CopyNumberVariation, SequenceMatching NeedsCompilation no git\_url https://git.bioconductor.org/packages/MEDIPS git\_branch RELEASE\_3\_19 git\_last\_commit 8bbaaa2 git\_last\_commit\_date 2024-04-30 Repository Bioconductor 3.19 Date/Publication 2024-09-15

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## Description

MEDIPS was developed for analyzing data derived from methylated DNA immunoprecipitation (MeDIP) experiments followed by sequencing (MeDIP-seq). Nevertheless, several functionalities may be applied to other types of sequencing data (e.g. differential coverage or testing the saturation of ChIP-seq data). MEDIPS addresses several aspects in the context of MeDIP-seq data analysis including basic data processing, several quality controls, normalization, and identification of differential coverage.

## **Details**

Package: MEDIPS
Type: Package
License: GPL (>=2)

LazyLoad: yes

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#### Author(s)

Lukas Chavez, Matthias Lienhard, Joern Dietrich Maintainer: Lukas Chavez <a href="mailto:clause.com/lienhard">clause.com/lienhard</a>, Joern Dietrich

#### References

Chavez L, Jozefczuk J, Grimm C, Dietrich J, Timmermann B, Lehrach H, Herwig R, Adjaye J., Computational analysis of genome-wide DNA methylation during the differentiation of human embryonic stem cells along the endodermal lineage, Genome Res. 2010 Oct;20(10):1441-50. Epub 2010 Aug 27.

COUPLINGset-class

COUPLINGset class and internal functions

#### **Description**

COUPLINGset class is used in the MEDIPS library to store and extract information generated during the creation of a coupling vector.

## **Objects from the Class**

Objects of the classes contain information about sequence pattern information, included chromosomes, and further parameter settings. A COUPLING SET object is created by the MEDIPS.couplingVector() function. According slots will be filled during the workflow.

## Slots

```
genome_name: Object of class "character": the reference genome
window_size: Object of class "numeric": the window size for the genome vector
chr_names: Object of class "character": the names of the chromosomes included within the
    MEDIPS/COUPLING SET
chr_lengths: Object of class "numeric": the lengths of the chromosomes included within the
    MEDIPS/COUPLING SET
seq_pattern: Object of class "character": the sequence pattern (e.g. CG)
genome_CF: Object of class "numeric": the coupling factor at the genomic bins
number_pattern: Object of class "numeric": the total number of sequence pattern
```

## Methods

```
genome_name signature(object = "COUPLINGset"): extracts the reference genome of the COU-
PLING SET
window_size signature(object = "COUPLINGset"): extracts the window size from the win-
dow_size slot COUPLING SET
```

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chr\_names signature(object = "COUPLINGset"): extracts the names of the chromosomes included within the COUPLING SET

chr\_lengths signature(object = "COUPLINGset"): extracts the length of the chromosomes included within the COUPLING SET

seq\_pattern signature(object = "COUPLINGset"): extracts the sequence pattern (e.g. CpG)

genome\_CF signature(object = "COUPLINGset"): extracts the coupling factor at the genomic
bins

number\_pattern signature(object = "COUPLINGset"): extracts the total number of sequence
pattern

show signature(object = "COUPLINGset"): prints a summary of the COUPLING SET object
content

#### Author(s)

Lukas Chavez, Matthias Lienhard, Joern Dietrich

## **Examples**

```
showClass("COUPLINGset")
```

MEDIPS.addCNV

Function to run a copy number variation analysis.

## Description

Function calculates a CNV analysis based on two INPUT SETs by employing the DNAcopy package. The results are attached to a provided result table.

## Usage

```
MEDIPS.addCNV(ISet1, ISet2, results, cnv.Frame=1000)
```

#### **Arguments**

ISet1 First group of INPUT SETsISet2 Second group of INPUT SETs

results result table as returned by the MEDIPS.meth function

cnv.Frame window size used for calculating CNVs. Can be of different size than the result

table.

#### Value

The result table with an additional column containing DNAcopy's log-ratio.

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#### Author(s)

Joern Dietrich

## **Examples**

```
library(MEDIPSData)
library("BSgenome.Hsapiens.UCSC.hg19")

bam.file.hESCs.Input = system.file("extdata", "hESCs.Input.chr22.bam", package="MEDIPSData")

bam.file.DE.Input = system.file("extdata", "DE.Input.chr22.bam", package="MEDIPSData")

hESCs.Input = MEDIPS.createSet(file=bam.file.hESCs.Input, BSgenome="BSgenome.Hsapiens.UCSC.hg19", extend=250, shDE.Input = MEDIPS.createSet(file=bam.file.DE.Input, BSgenome="BSgenome.Hsapiens.UCSC.hg19", extend=250, shift=0, data(resultTable)

resultTable = MEDIPS.addCNV(cnv.Frame=10000, ISet1=hESCs.Input, ISet2=DE.Input, results=resultTable)

MEDIPS.correlation

Calculates pairwise Pearson correlations between provided MEDIPS
```

## Description

The function calculates genome wide Pearson correlations between all pairs of provided MEDIPS SETs.

## Usage

```
MEDIPS.correlation(MSets=NULL, plot = T, method="spearman")
```

## **Arguments**

MSets a concatenated set of MEDIPS SETs

**SETs** 

plot if specified, the correlation will be depicted as a scatter plot

method default: spearman; alternatives: kendall, spearman

#### Value

a correlation matrix

#### Author(s)

Lukas Chavez

#### **Examples**

```
library(MEDIPSData)
data(hESCs_MeDIP)
data(DE_MeDIP)

correlation = MEDIPS.correlation(MSets=c(hESCs_MeDIP[[1]], DE_MeDIP[[1]]), plot = FALSE)
```

MEDIPS. coupling Vector Calculates the sequence pattern densities at genome wide windows.

## Description

The function calculates the local densities of a defined sequence pattern (e.g. CpGs) and returns a COUPLING SET object which is necessary for normalizing MeDIP data.

## Usage

```
MEDIPS.couplingVector(pattern="CG", ref0bj=NULL)
```

#### **Arguments**

pattern defines the sequence pattern, e.g. CG for CpGs.

ref0bj a MEDIPS Set or MEDIPS ROI Set that serves as reference for the genome and

window parameters.

## Value

A COUPLING SET object.

## Author(s)

Lukas Chavez

## Examples

```
library("MEDIPSData")
library("BSgenome.Hsapiens.UCSC.hg19")

data(hESCs_MeDIP)
CS = MEDIPS.couplingVector(pattern="CG", refObj=hESCs_MeDIP)
```

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MEDIPS.CpGenrich Calculates CpG enrichment of provided short reads compared to the reference genome.	MEDIPS.CpGenrich	Calculates CpG enrichment of provided short reads compared to the reference genome.
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## **Description**

As a quality check for the enrichment of CpG rich DNA fragments obtained by the immunoprecipitation step of a MeDIP experiment, this function provides the functionality to calculate CpG enrichment values. The main idea is to check, how strong the regions are enriched for CpGs compared to the reference genome. For this, the function counts the number of Cs, the number of Gs, the number CpGs, and the total number of bases within the stated reference genome. Subsequently, the function calculates the relative frequency of CpGs and the observed/expected ratio of CpGs present in the reference genome. Additionally, the function calculates the same for the DNA sequences underlying the given regions. The final enrichment values result by dividing the relative frequency of CpGs (or the observed/expected value, respectively) of the regions by the relative frequency of CpGs (or the observed/expected value, respectively) of the reference genome.

## Usage

MEDIPS.CpGenrich(file=NULL, BSgenome=NULL, extend=0, shift=0, uniq=1e-3, chr.select=NULL, paired=F)

#### **Arguments**

file	Path and file name of the input data
BSgenome	The reference genome name as defined by BSgenome
extend	defines the number of bases by which the region will be extended before the genome vector is calculated. Regions will be extended along the plus or the minus strand as defined by their provided strand information.
shift	As an alternative to the extend parameter, the shift parameter can be specified. Here, the reads are not extended but shifted by the specified number of nucleotides with respect to the given strand infomation. One of the two parameters extend or shift has to be 0.
uniq	The uniq parameter determines, if all reads mapping to exactly the same genomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value $(1 > \text{uniq} > 0)$ (deafult: 1e-3).
chr.select	only data at the specified chromosomes will be processed.
paired	option for paired end reads

#### Value

regions.CG the numbe of CpGs within the regions regions.C the number of Cs within the regions

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```
the number of Gs within the regions
regions.G
regions.relH
                 the relative frequency of CpGs within the regions
regions.GoGe
                  the observed/expected ratio of CpGs within the regions
genome.CG
                 the numbe of CpGs within the reference genome
genome.C
                  the number of Cs within the reference genome
                  the number of Gs within the reference genome
genome.G
genome.relH
                 the relative frequency of CpGs within the reference genome
genome.GoGe
                  the observed/expected ratio of CpGs within the reference genome
enrichment.score.relH
                 regions.relH/genome.relH
enrichment.score.GoGe
                 regions.GoGe/genome.GoGe
```

#### Author(s)

Joern Dietrich and Matthias Lienhard

## **Examples**

```
library(MEDIPSData)
library("BSgenome.Hsapiens.UCSC.hg19")
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
#er=MEDIPS.CpGenrich(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", chr.select="chr22"
```

MEDIPS.createROIset Creates a MEDIPS ROI SET by reading a suitable input file

## Description

Reads the input file and calculates the short read coverage (counts) for the specified regions of interest(ROI). After reading of the input file, the MEDIPS ROI SET contains information about the input file name, the dependent organism, the chromosomes included in the input file, the length of the included chromosomes (automatically loaded), the number of regions, and a GRange object of the ROIs.

#### Usage

MEDIPS.createROIset(file=NULL, ROI=NULL, extend=0, shift=0, bn=1, BSgenome=NULL, uniq=1e-3, chr.select

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#### **Arguments**

file Path and file name of the input data

ROI Data.frame with columns "chr", "start", "end" and "name" of regions of interest

extend defines the number of bases by which the region will be extended before the

genome vector is calculated. Regions will be extended along the plus or the

minus strand as defined by their provided strand information.

shift As an alternative to the extend parameter, the shift parameter can be specified.

Here, the reads are not extended but shifted by the specified number of nucleotides with respect to the given strand infomation. One of the two parameters

extend or shift has to be 0.

bn Number of bins per ROI

BSgenome The reference genome name as defined by BSgenome

uniq The uniq parameter determines, if all reads mapping to exactly the same ge-

nomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value (1 > uniq > 0) (deafult: 1e-3). The smaller the p-value, the more reads at the same genomic

position are potentially allowed.

chr.select only data at the specified chromosomes will be processed.

paired option for paired end reads

sample\_name name of the sample to be stored with the MEDIPSROI SET.

isSecondaryAlignment

option to import only primary alignments.

simpleCigar option to import only alignments with simple Cigar string.

#### Value

An object of class MEDIPSroiSet.

#### Author(s)

Lukas Chavez and Matthias Lienhard

#### **Examples**

```
library("BSgenome.Hsapiens.UCSC.hg19")
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
rois=data.frame(chr=c("chr22","chr22"), start=c(19136001, 19753401), stop=c(19136200, 19753500), ID=c("ID_1", "I
MSet=MEDIPS.createROIset(file=bam.file.hESCs.Rep1.MeDIP,ROI=rois, BSgenome="BSgenome.Hsapiens.UCSC.hg19", exter
```

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MEDIPS.createSet Creates a MEDIPS SET by reading a suitable input file

## **Description**

Reads the input file and calculates genome wide short read coverage (counts) at the specified window size. After reading of the input file, the MEDIPS SET contains information about the input file name, the dependent organism, the chromosomes included in the input file, the length of the included chromosomes (automatically loaded), and the number of regions.

## Usage

MEDIPS.createSet(file=NULL, extend=0, shift=0, window\_size=300, BSgenome=NULL, uniq=1e-3, chr.select=

## **Arguments**

file Path and file name of the input data

BSgenome The reference genome name as defined by BSgenome

extend defines the number of bases by which the region will be extended before the

genome vector is calculated. Regions will be extended along the plus or the

minus strand as defined by their provided strand information.

shift As an alternative to the extend parameter, the shift parameter can be specified.

Here, the reads are not extended but shifted by the specified number of nucleotides with respect to the given strand infomation. One of the two parameters

extend or shift has to be 0.

uniq The uniq parameter determines, if all reads mapping to exactly the same ge-

nomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value (1 > uniq > 0) (deafult: 1e-3). The smaller the p-value, the more reads at the same genomic

position are potentially allowed.

chr. select only data at the specified chromosomes will be processed.

window\_size defines the genomic resolution by which short read coverage is calculated.

paired option for paired end reads

sample\_name name of the sample to be stored with the MEDIPS SET.

isSecondaryAlignment

option to import only primary alignments.

simpleCigar option to import only alignments with simple Cigar string.

#### Value

An object of class MEDIPSset.

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#### Author(s)

Lukas Chavez, Mathias Lienhard, Isaac Lopez Moyado

## **Examples**

```
library("BSgenome.Hsapiens.UCSC.hg19")
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
```

MSet=MEDIPS.createSet(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", chr.select="chr22"

MEDIPS.exportWIG

Exports count, rpkm, or sequence pattern densities into a wiggle file.

## Description

The function allows for exporting the calculated methylation values (counts or rpkm) or sequence pattern densities from a MEDIPS or COUPLING SET into a wiggle (WIG) file. The wiggle file will contain values for all genomic windows of the genome/coupling vector and can be used for data visualization using appropriate genome browsers. Either a MEDIPS SET (parameter MSet) or a COUPLING SET (parameter CSet) has to be given.

## Usage

```
MEDIPS.exportWIG(Set=NULL, CSet=NULL, file=NULL, format="rpkm", descr="")
```

## Arguments

Set	has to be a MEDIPS SET object. Required when the parameter 'format' is 'count', 'rpkm', or 'rms'.
CSet	has to be a COUPLING SET object. Required when the parameter 'format' is 'pdensity' or 'rms'.
file	defines the name of the exported file
format	if set to "count", there must be a MEDIPS SET at 'Set'. The number of overlapping (extended) short reads per window will be exported. if set to "rpkm", there must be a MEDIPS SET at 'Set'. The rpkm values will be exported (default). If set to "pdensity", there must be a COUPLING SET at 'CSet'. The pattern

ping (extended) short reads per window will be exported. if set to "rpkm", there must be a MEDIPS SET at 'Set'. The rpkm values will be exported (default). If set to "pdensity", there must be a COUPLING SET at 'CSet'. The pattern densities (counts per window) will be exported (parameter Set will be ignored). If set to 'rms', there must be a MEDIPS SET at 'Set' and a corresponding COUPLING SET at 'CSet'. The CpG density normalized methylatin estimates will be exported.

be exported.

descr the exported wiggle file will include a track name and description that will be

visualized by the utilized genome browser. Both, track name and description

will be the same as defined here.

## Value

the funtion exports the specified data from the MEDIPS or COUPLING SET into the stated file

## Author(s)

Lukas Chavez

## **Examples**

```
library("BSgenome.Hsapiens.UCSC.hg19")
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
MSet=MEDIPS.createSet(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", chr.select="chr22"
MEDIPS.exportWIG(Set=MSet, file="hESCs.Rep1.wig", format="rpkm", descr="hESCs.Rep1")
```

MEDIPS.getAnnotation Funtion to fetch annotations from biomaRt.

#### **Description**

The function receives predifined annotations from ensembl biomaRt for subsequent annotation of a result table.

#### Usage

MEDIPS.getAnnotation(host="www.ensembl.org",dataset=c("hsapiens\_gene\_ensembl","mmusculus\_gene\_ensem

## Arguments

host	BioMart database host you want to connect to. For current ensembl version, use "www.ensembl.org". For other versions, set to the respective archive host, e.g. "may2012.archive.ensembl.org" for Ensembl 67 Please ensure that the ensembl version is compatible to the used genome version.
dataset	The dataset you want to use. To see the different datasets available within a biomaRt you can e.g. do: mart = useMart('ensembl'), followed by listDatasets(mart).
annotation	Type of annotation you want to retrieve. You can select "EXON" for exonic regions, "GENE" for gene regions including introns and "TSS" for regions at the transcirption start site.
tssSz	Defines the TSS region: start and end position relative to the strand and position of the transcript.
chr	Chromosome names for which the annotations should be filtered.

#### Value

The MEDIPS.getAnnotation function returns a list of annotation tables where each table consists of

id the id of the annotation

chr the chromosome of the annotation start the start position (5') of the annotation end the end position (3') of the annotation

## Author(s)

Joern Dietrich and Matthias Lienhard

## **Examples**

```
#homo sapiens, current ensembl version
#annotation_hs = MEDIPS.getAnnotation(dataset="hsapiens_gene_ensembl", annotation="TSS", chr=c("chr22"),tssSz=c
#mus musculus, ensembl version 58 (mm9)
#annotation_mm9 = MEDIPS.getAnnotation(host="may2010.archive.ensembl.org",dataset="mmusculus_gene_ensembl", annotation_mm9
```

MEDIPS.mergeFrames Merges genomic coordinates of neighboring windows into one super-

sized window

## Description

After having filtered the result table returned by the MEDIPS.meth function using the MEDIPS.selectSig function, there might be neighboring significant frames. For these cases it is worthwhile to merge neighbouring regions into one supersized frame.

## Usage

```
MEDIPS.mergeFrames(frames=NULL, distance=1)
```

## **Arguments**

frames is a filtered result table received by the MEDIPS.selectSig function.

distance allows an according number of bases as a gap between neighboring significant

windows to be merged. The default value is 1 in order to merge adjacent win-

dows.

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#### Value

The remaining distinct frames are represented only by their genomic coordinates within the returned results table

chromosome the chromosome of the merged frame start the start position of the merged frame stop the stop position of the merged frame ID a numbered ID of the merged frame

The result table does not contain any merged significant values.

#### Author(s)

Lukas Chavez

#### **Examples**

```
regions=as.data.frame(list(chr=c("chr22", "chr22"), start=c(1001, 1501), stop=c(1500,1750)))
regions.merged=MEDIPS.mergeFrames(regions)
regions.merged
```

MEDIPS.mergeSets

Creates one merged MEDIPS SET out of two.

## Description

A MEDIPS SET contains a genome vector which is the count coverage at genome wide windows. Moreover, the MEDIPS SET stores the total number of reads given for calculating the genome vector. Two MEDIPS SETs can be merged whenever they have been constructed based on the same reference genome, the same set of chromosomes and for the same window size. The returned MEDIPS SET will contain a genome vector where at each window the counts of both given MEDIPS SETs are added. In addition, the total number of reads will be the sum of both given MEDIPS SETs. Please note, several other attributes like the extend or shift value can be different in both of the given MEDIPS SETs and will be empty in the merged MEDIPS SET. The merged MEDIPS SET will not contain any path to a concrete input file anymore and therefore, cannot be used for the MEDIPS.addCNV function anymore.

## Usage

```
MEDIPS.mergeSets(MSet1=NULL, MSet2=NULL, name="Merged Set")
```

#### **Arguments**

MSet1	A MEDIPS SET object as created by the MEDIPS.createSet function
MSet2	A MEDIPS SET object as created by the MEDIPS.createSet function
name	The new sample name of the merged MEDIPS SET

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#### Author(s)

Lukas Chavez

## **Examples**

```
library(MEDIPSData)
data(hESCs_Input)
data(DE_Input)

merged_Set = MEDIPS.mergeSets(hESCs_Input, DE_Input, name="Merged_input")

merged_Set
```

MEDIPS.meth

Funtion summarizes coverage profiles for given MEDIPS SETs and allows to calculate differential coverage and copy number vartiation, if applicable.

## Description

The function summarizes coverage profiles (counts, rpkm) for given MEDIPS SETs at the slots MSet1, MSet2, ISet1, and ISet1. In case the parameter MeDIP is set to TRUE and a COUPLING SET was provided at the slot CS, the function will calculate CpG density normalized methylation profiles (relative methylation score, rms) for the MEDIPS SETs at the slots MSet1 and MSet2. In case two groups of MEDIPS SETs have been provided at MSet1 and MSet2, the function will calculate differential coverage. In case two groups of MEDIPS SETs have been provided at ISet1 and ISet2 and the parameter CNV was set to TRUE, the function will calculate copy number variation. The function allows for processing a variable number of provided MEDIPS SETs and therefore, the returned matrix is of variable length.

#### Usage

```
MEDIPS.meth(MSet1 = NULL, MSet2 = NULL, CSet = NULL, ISet1 = NULL, ISet2 = NULL, chr = NULL, p.adj="bonfe"
```

## **Arguments**

MSet1	has to be one or a concatenated list of MEDIPS SET objects (the control replicates)
MSet2	has to be one or a concatenated list of MEDIPS SET objects (the treatment data) or empty
CSet	has to be a COUPLING SET object (must fit the given MEDIPS SET objects with respect to reference genome and represented chromosomes)
ISet1	has to be one or a concatenated list of Input derived MEDIPS SET objects (general Input data or Inputs from the control replicates) or empty
ISet2	has to be one or a concatenated list of Input derived MEDIPS SET objects (Inputs from the treatment replicates) or empty

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chr specify one or several chromosomes (e.g. c("chr1", "chr2")), if only a subset of

available chromosomes have to be processed.

p. adj in order to correct p.values derived from the differential coverage analysis for

multiple testing, MEDIPS uses Rs' p.adjust function. Therefore, the following methods are available: holm, hochberg, hommel, bonferroni (default), BH, BY,

fdr, none.

diff.method method for calculating differential coverage. Available methods: ttest (default)

and edgeR.

CNV In case there are INPUT SETs provided at both Input slots (i.e. ISet1 and ISet2),

copy number variation will be tested by applying the package DNAcopy to the window-wise log-ratios calculated based on the the means per group. By setting CNV=F this function will be disabled (default: CNV=TRUE). Please note, there is the function MEDIPS.addCNV which allows to run the CNV analysis on two

groups of INPUT SETs using another (typically increased) window size.

MeDIP This parameter determines, whether for the MEDIPS SETs given at the slots

MSet1 and MSet2, CpG density dependent normalization values (rms and prob)

will be calculated (default: MeDIP=TRUE).

minRowSum threshold for the sum of counts in a window for the staistical test (default=10).

diffnorm This parameter defines which normalisation method is applied prior to testing

for differential enrichment between conditions (default='tmm'). tmm, quantile and none are possible when diff.method=edgeR while rpkm and rms are possible

when diff.method=ttest.

#### Value

Chr the chromosome of the ROI
Start the start position of the ROI
Stop the stop position of the ROI

CF the number of CpGs in the window

\*counts a variable number of columns (according to the number of provided MEDIPS

SETs) containing for each set the number of (extended/shifted) reads that over-

lap with the window.

\*rpkm a variable number of columns (according to the number of provided MEDIPS

SETs) containing for each set the rpkm value of the window.

\*rms optional (if MeDIP=TRUE): a variable number of columns (according to the

number of provided MEDIPS SETs) containing for each set the rms value of the

window.

\*counts optional (if INPUT SETs given): a variable number of columns (according to

the number of provided INPUT SETs) containing for each set the number of

(extended/shifted) reads that overlap with the window.

\*rpkm optional (if INPUT SETs given): a variable number of columns (according to

the number of provided INPUT SETs) containing for each set the rpkm value of

the window.

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MSets1.counts.mean

optional (if more than one MEDIPS SET given): the mean count over all MEDIPS SETs at MSet1.

MSets1.rpkm.mean

optional (if more than one MEDIPS SET given): the mean rpkm value over all MEDIPS SETs at MSet1.

MSets1.rms.mean

optional (if more than one MEDIPS SET given): the mean rms value over all MEDIPS SETs at MSet1.

MSets2.counts.mean

optional (if more than one MEDIPS SET given): the mean count over all MEDIPS SETs at MSet2.

MSets2.rpkm.mean

optional (if more than one MEDIPS SET given): the mean rpkm value over all MEDIPS SETs at MSet2.

MSets2.rms.mean

optional (if more than one MEDIPS SET given): the mean rms value over all MEDIPS SETs at MSet2.

ISets1.counts.mean

optional (if more than one INPUT SET given): the mean count over all INPUT SETs at ISet1.

ISets1.rpkm.mean

optional (if more than one INPUT SET given): the mean rpkm value over all INPUT SETs at ISet1.

ISets2.counts.mean

optional (if more than one INPUT SET given): the mean count over all INPUT SETs at ISet2.

ISets2.rpkm.mean

optional (if more than one INPUT SET given): the mean rpkm value over all INPUT SETs at ISet2.

edgeR.logFC optional (if diff.method=edgeR): log fold change between MSet1 and MSet2 as returned by edgeR.

edgeR.logCPM optional (if diff.method=edgeR): logCPM between MSet1 and MSet2 as returned by edgeR.

edgeR.p.value optional (if diff.method=edgeR): p.value as returned by edgeR.

edgeR.adj.p.value

optional (if diff.method=edgeR): adjusted p.value as calculated by the p.adjust function using edgeR's p.values as input.

score.log2.ratio

optional (if diff.method=ttest): log2 fold change between the means of the groups MSet1 and MSet2.

score.p.value optional (if diff.method=ttest): p.value as returned by the t.test function. score.adj.p.value

optional (if diff.method=ttest): adjusted p.value as calculated by the p.adjust function using the ttest p.values as input.

score optional (if diff.method=ttest): score = (-log10(score.p.value)\*10)\*log(score.log2.ratio)

CNV.log2.ratio optional (if two INPUT SETs given and CNV=TRUE): the log2 ratio for segments as calculated by the DNAcopy package.

#### Author(s)

Lukas Chavez, Matthias Lienhard, Joern Dietrich

#### **Examples**

```
library(MEDIPSData)
data(hESCs_MeDIP)
data(DE_MeDIP)
data(hESCs_Input)
data(DE_Input)
data(CS)
```

resultTable = MEDIPS.meth(MSet1 = hESCs\_MeDIP, MSet2 = DE\_MeDIP, CSet = CS, ISet1 = hESCs\_Input, ISet2 = DE\_Input, c

MEDIPS.plotCalibrationPlot

Creates the calibration plot.

## **Description**

Visualizes the dependency between MeDIP-seq signals and CpG densities together with the calcibration curve and the results of the linear modelling.

#### Usage

MEDIPS.plotCalibrationPlot(MSet=NULL, ISet=NULL, CSet=NULL, plot\_chr="all", rpkm=T, main="Calibration")

#### Arguments

ISet an INPUT SET (i.e. a MEDIPS SET created from Input sequening data)

CSet an according COUPLING SET object

plot\_chr default="all". It is recommended to call a graphics device (e.g. png("calibrationPlot.png"))

before calling the plot command, because R might not be able to plot the full

amount of data in reasonable time.

rpkm can be either TRUE or FALSE. If set to TRUE, the methylation signals will be

transformed into rpkm before plotted. The coupling values remain untouched. It is necessary to set rpkm=T, if both, a MSet and an ISet are given and plotted

at the same time.

main The title of the calibration plot.

xrange The signal range of the calibration curve typically falls into a low signal range.

By setting the xrange parameter to TRUE, the calibration plot will visualize the

low signal range only.

#### Value

The calibration plot will be visualized.

#### Author(s)

Lukas Chavez, Matthias Lienhard

#### **Examples**

```
library(MEDIPSData)
data(hESCs_MeDIP)
data(CS)
```

MEDIPS.plotCalibrationPlot(CSet=CS, main="Calibration Plot", MSet=hESCs\_MeDIP[[1]], plot\_chr="chr22", rpkm=TRUE

 ${\tt MEDIPS.plotSaturation} \ \ \textit{Function plots the results of the MEDIPS. saturation Analysis function}.$ 

#### **Description**

The results of the saturation analysis will be visualized by the function.

## Usage

```
MEDIPS.plotSaturation(saturationObj = NULL, main="Saturation analysis")
```

## Arguments

saturationObj The saturation results object returned by the MEDIPS.saturationAnalysis func-

tion

main The title of the coverage plot.

#### Value

The coverage plot will be visualized.

#### Author(s)

Lukas Chavez

## Examples

```
library(MEDIPSData)
library(BSgenome.Hsapiens.UCSC.hg19)
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
sr=MEDIPS.saturation(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", uniq=1e-3, extend=MEDIPS.plotSaturation(saturationObj = sr, main="Saturation analysis")
```

MEDIPS.plotSeqCoverage

Function plots the results of the MEDIPS.seqCoverage function.

## **Description**

The results of the sequence pattern coverage analysis will be visualized in two possible ways.

## Usage

```
MEDIPS.plotSeqCoverage(seqCoverageObj=NULL, main=NULL, type="pie", cov.level = c(0,1,2,3,4,5), t="Inf
```

## Arguments

seqCoverageObj The coverage results object returned by the MEDIPS.seqCoverage function.

main The title of the coverage plot.

type there are two types of visualization. The pie chart (default) illustrates the frac-

tion of CpGs covered by the given reads at different coverage level (see also the parameter cov.level). As an alternative, a histogram over all coverage level can

be ploted ("hist").

cov.level The pie chart illustrates the fraction of CpGs covered by the given reads accord-

ing to their coverage level. The visualized coverage levels can be adjusted by

the cov.level parameter.

t specifies the maximal coverage depth to be plotted, if type="hist"

## Value

The sequence pattern coverage plot will be visualized.

#### Author(s)

Lukas Chavez

## **Examples**

```
library(MEDIPSData)
library(BSgenome.Hsapiens.UCSC.hg19)
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")

cr=MEDIPS.seqCoverage(file=bam.file.hESCs.Rep1.MeDIP, pattern="CG", BSgenome="BSgenome.Hsapiens.UCSC.hg19", chr

MEDIPS.plotSeqCoverage(seqCoverageObj=cr, main="Sequence pattern coverage", type="pie", cov.level = c(0,1,2,3,4,5)
```

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MEDIPS.saturation	Function calculates the saturation/reproducibility of the provided IP-Seq data.
	seq uuu.

## Description

The saturation analysis addresses the question, whether the number of short reads is sufficient to generate a saturated and reproducible coverage profile of the reference genome. The main idea is that an insufficent number of short reads will not result in a saturated methylation profile. Only if there is a sufficient number of short reads, the resulting genome wide coverage profile will be reproducible by another independent set of a similar number of short reads.

## Usage

MEDIPS.saturation(file=NULL, BSgenome=NULL, nit=10, nrit=1, empty\_bins=TRUE, rank=FALSE, extend=0, sha

## Arguments

0	
file	Path and file name of the IP data
BSgenome	The reference genome name as defined by BSgenome
nit	defines the number of subsets created from the full sets of available regions (default= $10$ )
nrit	methods which randomly select data entries may be processed several times in order to obtain more stable results. By specifying the nrit parameter (default=1) it is possible to run the saturation analysis several times. The final results returned to the saturation results object are the averaged results of each random iteration step.
empty_bins	can be either TRUE or FALSE (default TRUE). This parameter effects the way of calculating correlations between the resulting genome vectors. A genome vector consists of concatenated vectors for each included chromosome. The size of the vectors is defined by the bin_size parameter. If there occur genomic bins which contain no overlapping regions, neither from the subsets of A nor from the subsets of B, these bins will be neglected when the parameter is set to FALSE.
rank	can be either TRUE or FALSE (default FALSE). This parameter also effects the way of calculating correlations between the resulting genome vectors. If rank is set to TRUE, the correlation will be calculated for the ranks of the windows instead of considering the counts (Spearman correlation). Setting this parameter to TRUE is a more robust approach that reduces the effect of possible occuring outliers (these are windows with a very high number of overlapping regions) to the correlation.
extend	defines the number of bases by which the region will be extended before the genome vector is calculated. Regions will be extended along the plus or the minus strand as defined by their provided strand information. Please note, the extend and shift parameter are mutual exclusive.

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shift defines the number of bases by which the region will be shifted before the

genome vector is calculated. Regions will be shifted along the plus or the minus strand as defined by their provided strand information. Please note, the extend

and shift parameter are mutual exclusive.

window\_size defines the size of genome wide windows and therefore, the size of the genome

vector.

uniq The uniq parameter determines, if all reads mapping to exactly the same ge-

nomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value (1 > uniq > 0) (deafult: 1e-3). The smaller the p-value, the more reads at the same genomic

position are potentially allowed.

chr. select specify a subset of chromosomes for which the saturation analysis is performed.

paired option for paired end reads

isSecondaryAlignment

option to import only primary alignments.

simpleCigar option to import only alignments with simple Cigar string.

#### Value

distinctSets Contains the results of each iteration step (row-wise) of the saturation analysis.

The first column is the number of considered regions in each set, the second column is the resulting pearson correlation coefficient when comparing the two

independent genome vectors.

estimation Contains the results of each iteration step (row-wise) of the estimated saturation

analysis. The first column is the number of considered regions in each set, the second column is the resulting pearson correlation coefficient when comparing

the two independent genome vectors.

distinctSets the total number of available regions

maxEstCor contains the best pearson correlation (second column) obtained by considering

the artifically doubled set of reads (first column)

distinctSets contains the best pearson correlation (second column) obtained by considering

the total set of reads (first column)

#### Author(s)

Lukas Chavez

#### **Examples**

```
library(MEDIPSData)
```

```
library(BSgenome.Hsapiens.UCSC.hg19)
```

```
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")
```

sr=MEDIPS.saturation(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", uniq=1e-3, extend=

MEDIPS.selectROIs 23

MEDIPS.selectROIs	Selects row-wise subsets of a result table as returned by the MEDIPS.meth function.

## Description

MEDIPS provides the functionality to select subsets of the result matrix returned by the MEDIPS.meth function according to any given set of regions of interest (ROIs).

## Usage

```
MEDIPS.selectROIs(results=NULL, rois=NULL, columns=NULL, summarize=NULL)
```

## Arguments

results	a result table as returned by the function MEDIPS.meth
rois	A matrix containing genomic coordinates of any regions of interest.
columns	Only selected columns will be returned as determined by the columns parameter. It is possible to specify one or more concrete column names, please see an example below.
summarize	By setting summarize=NULL (default) all windows included in the genomic ranges of the given ROIs will be returned. As an alternative, it is possible to calculate mean (summarize = "avg") or sum (summarize = "sum") values over the individual windows included in each ROI, or to select only the most significant window within each given ROI (summarize="minP").

## Author(s)

Lukas Chavez, Matthias Lienhard

library(MEDIPSData)

## **Examples**

```
data(resultTable)
rois=data.frame(chr=c("chr22","chr22"), start=c(19136001, 19753401), stop=c(19136200, 19753500), ID=c("ID_1", "Identification of the columns of the
```

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MEDIPS.selectSig	Selects windows which show significant differential coverage between two MEDIPS SETs from a resultTable (as returned by the function MEDIPS.meth).

## Description

Based on the results table returned by the MEDIPS.meth function, the function selects windows which show significant differential coverage between the two groups of MEDIPS SETs. Selection of significant windows follows according to the specification of the available parameters.

## Usage

MEDIPS.selectSig(results=NULL, p.value=0.01, adj=T, ratio=NULL, bg.counts=NULL, CNV=F)

#### **Arguments**

results	specifies the result table derived from the MEDIPS.meth function.
p.value	this is the p.value threshold as calculated either by the ttest or edgeR method
adj	this parameter specifies whether the p.value or the adjusted p.values is considered
ratio	this parameter sets an additional thresold for the ratio where the ratio is either score.log2.ratio or edgeR.logFC depending on the previously selected method. Please note, the specified value will be transformed into log2 internally.
bg.counts	as an additional filter parameter, it is possible to require a minimal number of reads per window in at least one of the MEDIPS SET groups. For this, the mean of counts per group is considered. The parameter bg.counts can either be a concrete integer or an appropriate column name of the result table. By specifying a column name, the 0.95 quantile of the according genome wide count distribution is determined and used as a minimal background threshold (please note, only count columns are reasonable).
CNV	The information on CNVs present in the samples of interest can be used for correcting differential coverage observed in the corresponding IP data (e.g. MeDIP or ChIP data). In case Input data has been provided for both conditions, MEDIPS is capable of calculating genome wide CNV ratios by employing the package DNAcopy. In case the parameter CNV is set to TRUE, MEDIPS will subtract the CNV ratio from the IP ratio. Subsequently, only genomic windows having a CNV corrected IP ratio higher than the specified ratio threshold (specification of the ratio parameter is required in this case) will be considered as windows with sufficient differential IP coverage.

## Author(s)

Lukas Chavez, Matthias Lienhard

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#### **Examples**

```
library(MEDIPSData)
data(resultTable)
```

sig = MEDIPS.selectSig(results=resultTable, p.value=0.05, adj=TRUE, ratio=NULL, bg.counts=NULL, CNV=FALSE)

MEDIPS.seqCoverage

The function identifies the number of CpGs (or any other predefined sequence pattern) covered by the given short reads.

## Description

The main idea of the sequence pattern coverage analysis is to test the number of CpGs (or any other predefined sequence pattern) covered by the given short reads and to test the depth of coverage.

## Usage

MEDIPS.seqCoverage(file = NULL, BSgenome = NULL, pattern = "CG", extend = 0, shift = 0, uniq = 1e-3, chr.

## **Arguments**

simpleCigar

- 5	50222000	
	file	Path and file name of the input data
	BSgenome	The reference genome name as defined by BSgenome
	pattern	defines the sequence pattern, e.g. CG for CpGs.
	extend	defines the number of bases by which the region will be extended before the genome vector is calculated. Regions will be extended along the plus or the minus strand as defined by their provided strand information. Please note, the extend and shift parameter are mutual exclusive.
	shift	defines the number of bases by which the region will be shifted before the genome vector is calculated. Regions will be shifted along the plus or the minus strand as defined by their provided strand information. Please note, the extend and shift parameter are mutual exclusive.
	uniq	The uniq parameter determines, if all reads mapping to exactly the same genomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value ( $1 > \text{uniq} > 0$ ) (deafult: 1e-3). The smaller the p-value, the more reads at the same genomic position are potentially allowed.
	chr.select	specify a subset of chromosomes for which the saturation analysis is performed.
	paired	option for paired end reads
isSecondaryAlignment		
		option to import only primary alignments.

option to import only alignments with simple Cigar string.

26 MEDIPS.setAnnotation

## Author(s)

Lukas Chavez

## **Examples**

```
library(MEDIPSData)
library(BSgenome.Hsapiens.UCSC.hg19)
bam.file.hESCs.Rep1.MeDIP = system.file("extdata", "hESCs.MeDIP.Rep1.chr22.bam", package="MEDIPSData")

cr = MEDIPS.seqCoverage(file=bam.file.hESCs.Rep1.MeDIP, BSgenome="BSgenome.Hsapiens.UCSC.hg19", pattern="CG", extended to the supplementary of the supplementa
```

MEDIPS.setAnnotation Funtion to annotate a matrix of genomic coordinates (i.e. a result table) by a given annotation object.

## **Description**

The function appends any annotation IDs included in the given annotation object to the given regions object. An annotation object can be retrived by the MEDIPS.getAnnotation function and the regions object is typically a (filtered) result table as returned by the MEDIPS.meth function. An annotation ID is appended to a genomic region if their genomic coordinates overlap by at least one base. There will be as many columns added to the regions object as overlapping annotations exist in the annotation object.

## Usage

MEDIPS.setAnnotation(regions, annotation, cnv=F)

## **Arguments**

regions a matrix that contains row-wise genomic regions, e.g. as a result of the MEDIPS.meth

function.

annotation the annotation data object contains the genomic coordinates of annotations. An

annotation object can be e.g. retrived by the MEDIPS.getAnnotation function.

cnv the MEDIPS.setAnnotation function is also internally used by the MEDIPS.addCNV

function which automatically sets this parameter to TRUE. Otherwise cnv should

be set to FALSE.

#### Value

The provided result object with added columns containing overlapping annotations.

## Author(s)

Joern Dietrich, Matthias Lienhard

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#### **Examples**

```
library(MEDIPSData)
data(resultTable)

sig = MEDIPS.selectSig(results=resultTable, p.value=0.05, adj=TRUE, ratio=NULL, bg.counts=NULL, CNV=FALSE)
sig = MEDIPS.mergeFrames(frames=sig, distance=1)
#ens_gene = MEDIPS.getAnnotation( annotation="GENE",chr="chr22")
#sig = MEDIPS.setAnnotation(regions=sig, annotation=ens_gene)
```

MEDIPSroiSet-class

MEDIPSroiSet class and internal functions

## **Description**

MEDIPSroiSet class is used in the MEDIPS library in order to store and extract objects and information of the specified regions of interest (ROI) from the input file as well as parameter settings specified during the workflow.

## **Objects from the Class**

Objects of the classes contain information about the provided short reads, MeDIP raw/count signals, and further parameter settings. A MEDIPS ROI SET object is created by the MEDIPS.createROIset() function. According slots will be filled during the workflow.

## **Slots**

```
genome_name: Object of class "character": the refernce genome
chr_names: Object of class "character": the names of the chromosomes included within the
     MEDIPS ROI SET
chr_lengths: Object of class "numeric": the lengths of the chromosomes included within the
     MEDIPS ROI SET
sample_name: Object of class "character": the name of the input file
path_name: Object of class "character": the path to the input file
number_regions: Object of class "numeric": the total number of included regions
genome_count: Object of class "numeric": the raw MeDIP-seq signals at the bins
extend: Object of class "numeric": the length of the reads after extension
shifted: Object of class "numeric": the number of bases by which the reads are shifted along
     the sequencing direction
uniq: Object of class "logical": determines if reads mapping to exactly the same genomic posi-
     tion should be replaced by only on representative
ROI: Object of class "GRanges": the genomic positions of the regions of interest
bin_number: Object of class "numeric": the number of bins per region
```

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#### Methods

- bin\_number signature(object = "MEDIPSroiSet"): extracts the number of bins per ROI the bin\_number slot of the MEDIPS ROI SET
- chr\_names signature(object = "MEDIPSroiSet"): extracts the names of the chromosomes included within the MEDIPS ROI SET
- chr\_lengths signature(object = "MEDIPSroiSet"): extracts the length of the chromosomes included within the MEDIPS ROI SET
- sample\_name signature(object = "MEDIPSroiSet"): extracts the name of the input file
- path\_name signature(object = "MEDIPSroiSet"): extracts the path to the input file
- number\_regions signature(object = "MEDIPSroiSet"): extracts the total number of included
   regions
- genome\_count signature(object = "MEDIPSroiSet"): extracts the raw MeDIP-Seq signals at
  the genomic bins
- extend signature(object = "MEDIPSroiSet"): extracts the number of bases by which the regions are extended
- show signature(object = "MEDIPSroiSet"): prints a summary of the MEDIPS SET object content
- shifted signature(object = "MEDIPSroiSet"): extracts the number of bases by which the regions are shifted
- uniq signature(object = "MEDIPSroiSet"): extracts the specified value for the uniq parameter
- rois signature(object = "MEDIPSroiSet"): extracts the GRange object containing the regions
   of interest
- **MEDIPS.calibrationCurve** signature(MSet = "MEDIPSroiSet", CSet="COUPLINGset"): internal function for calculating the calibration curve
- **MEDIPS.negBin** signature(MSet="MEDIPSroiSet", CSet="COUPLINGset"): internal function for calculating methylatiopn probabilities with respect to CpG density dependent negative binomial distributions
- **MEDIPS.pois** signature(MSet="MEDIPSroiSet", CSet="COUPLINGset"): internal function for calculating methylatiopn probabilities with respect to CpG density dependent poisson distributions
- **MEDIPS.rms** signature(MSet="MEDIPSroiSet", CSet="COUPLINGset"): internal function for calculating relative methylation scores

#### Author(s)

Lukas Chavez, Joern Dietrich

## **Examples**

showClass("MEDIPSroiSet")

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MEDIPSset-class

MEDIPSset class and internal functions

#### **Description**

MEDIPS set class is used in the MEDIPS library in order to store and extract objects and information from the input file as well as parameter settings specified during the workflow.

## **Objects from the Class**

Objects of the classes contain information about the provided short reads, MeDIP raw/count signals, and further parameter settings. A MEDIPS SET object is created by the MEDIPS genomeVector() function. According slots will be filled during the workflow.

#### **Slots**

```
genome_name: Object of class "character": the refernce genome
```

window\_size: Object of class "numeric": the window size for the genome vector

chr\_names: Object of class "character": the names of the chromosomes included within the MEDIPS/COUPLING SET

sample\_name: Object of class "character": the name of the input file

path\_name: Object of class "character": the path to the input file

number\_regions: Object of class "numeric": the total number of included regions

genome\_count: Object of class "numeric": the raw MeDIP-seq signals at the genomic bins

extend: Object of class "numeric": the length of the regions after extension

shifted: Object of class "numeric": the number of bases by which the reads are shifted along the sequencing direction

uniq: Object of class "logical": determines if all reads mapping to exactly the same genomic position should be kept (uniq = 0), replaced by only one representative (uniq = 1), or if the number of stacked reads should be capped by a maximal number of stacked reads per genomic position determined by a poisson distribution of stacked reads genome wide and by a given p-value (1 > uniq > 0).

#### Methods

window\_size signature(object = "MEDIPSset"): extracts the window size from the bin\_size
 slot of the MEDIPS SET

chr\_names signature(object = "MEDIPSset"): extracts the names of the chromosomes included
 within the MEDIPS SET

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chr\_lengths signature(object = "MEDIPSset"): extracts the length of the chromosomes included within the MEDIPS SET

- fragmentLength signature(object = "MEDIPSset"): extracts the estimated fragment length of
   the DNA fragments
- sample\_name signature(object = "MEDIPSset"): extracts the name of the input file
- path\_name signature(object = "MEDIPSset"): extracts the path to the input file
- number\_regions signature(object = "MEDIPSset"): extracts the total number of included regions
- genome\_count signature(object = "MEDIPSset"): extracts the raw MeDIP-Seq signals at the
   genomic bins
- extend signature(object = "MEDIPSset"): extracts the number of bases by which the regions
  are extended
- **show** signature(object = "MEDIPSset"): prints a summary of the MEDIPS SET object content
- shifted signature(object = "MEDIPSset"): extracts the number of bases by which the regions
  are shifted
- uniq signature(object = "MEDIPSset"): extracts the specified value for the uniq parameter
- **MEDIPS.GenomicCoordinates** signature(object = "MEDIPSset"): internal function for calculating coordinates for the genomic bins
- **MEDIPS.readRegionsFile** signature(object = "MEDIPSset"): internal function for reading short read information
- **MEDIPS.calibrationCurve** signature(object = "MEDIPSset"): internal function for calculating the calibration curve
- **MEDIPS.cnv** signature(object = "MEDIPSset"): internal function for calculating CNVs in case two groups of INPUT SETs have been provided to the MEDIPS.meth function
- **MEDIPS.diffMeth** signature(object = "MEDIPSset"): internal function for calculating differential coverage in case two groups of MEDIPS SETs have been provided to the MEDIPS.meth function
- **MEDIPS.getPositions** signature(object = "MEDIPSset"): internal function for receiving genomic coordinates of a given sequence pattern (e.g. CG)
- **MEDIPS.rms** signature(object = "MEDIPSset"): internal function for calculating relative methylation scores
- matNnotNA signature(object = "MEDIPSset"): internal function for vectorized calculation of
   the t.test
- matMin signature(object = "MEDIPSset"): internal function for vectorized calculation of the
   t.test
- matMax signature(object = "MEDIPSset"): internal function for vectorized calculation of the
   t.test

- matTtest signature(object = "MEDIPSset"): internal function for vectorized calculation of the
   t.test

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## Author(s)

Lukas Chavez, Joern Dietrich

# Examples

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