

Package ‘mosaics’

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Type Package

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Enhances parallel

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Description This package provides functions for fitting MOSAiCS and MOSAiCS-HMM, a statistical framework to analyze one-sample or two-sample ChIP-seq data of transcription factor binding and histone modification.

License GPL (>= 2)

URL http://groups.google.com/group/mosaics_user_group

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| | |
|-----------------|---|
| mosaics-package | <i>MOSAiCS (Model-based one and two Sample Analysis and Inference for ChIP-Seq)</i> |
|-----------------|---|

Description

This package provides functions for fitting MOSAiCS, a statistical framework to analyze one-sample or two-sample ChIP-seq data.

Details

| | |
|-----------|------------|
| Package: | mosaics |
| Type: | Package |
| Version: | 2.9.9 |
| Date: | 2016-03-15 |
| License: | GPL (>= 2) |
| LazyLoad: | yes |

This package contains four main classes, `BinData`, `MosaicsFit`, `MosaicsHMM`, and `MosaicsPeak`, which represent bin-level ChIP-seq data, MOSAiCS model fit, MOSAiCS-HMM model fit, and MOSAiCS peak calling results, respectively. This package contains ten main methods, `constructBins`, `readBins`, `mosaicsFit`, `mosaicsPeak`, `mosaicsFitHMM`, `mosaicsPeakHMM`, `extractReads`, `findSummit`, `adjustBoundary`, `filterPeak`. `constructBins` method constructs bin-level files from the aligned read file. `readBins` method imports bin-level data and construct `BinData` class object. `mosaicsFit` method fits a MOSAiCS model using `BinData` class object and constructs `MosaicsFit` class object. `mosaicsPeak` method calls peaks using `MosaicsFit` class object and construct `MosaicsPeak` class object. `mosaicsFitHMM` and `mosaicsPeakHMM` are designed to identify broad peaks and their functions correspond to `mosaicsFit` and `mosaicsPeak`, respectively. `mosaicsFitHMM` method fits a MOSAiCS-HMM model using `MosaicsFit` class object and constructs `MosaicsHMM` class object. `mosaicsPeakHMM` method calls MOSAiCS-HMM peaks using `MosaicsHMM` class object and construct `MosaicsPeak` class object. `extractReads`, `findSummit`, `adjustBoundary`, `filterPeak` methods postprocess MOSAiCS and MOSAiCS-HMM peaks using `MosaicsPeak` class object (incorporate read-level data, identify peak summits, adjust peak boundaries, and filter potential false positive peaks, respectively) and construct `MosaicsPeak` class object. `MosaicsPeak` class object can be exported as text files or transformed into data frame, which can be used for the downstream analysis. This package also provides methods for simple exploratory analysis.

The `mosaics` package companion website, <http://www.stat.wisc.edu/~keles/Software/mosaics/>, provides preprocessing scripts, preprocessed files for diverse reference genomes, and easy-to-follow instructions. We encourage questions or requests regarding `mosaics` package to be posted on our Google group, http://groups.google.com/group/mosaics_user_group. Please check the vignette for further details on the `mosaics` package and these websites.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles
Maintainer: Dongjun Chung <dongjun.chung@gmail.com>

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

`constructBins`, `readBins`, `mosaicsFit`, `mosaicsPeak`, `mosaicsFitHMM`, `mosaicsPeakHMM`, `extractReads`, `findSummit`, `adjustBoundary`, `filterPeak`, `BinData`, `MosaicsFit`, `MosaicsHMM`, `MosaicsPeak`.

Examples

```
## Not run:  
library(mosaicsExample)  
  
# example analysis workflow for ChIP-seq data of transcription factor binding
```

```

# (STAT1 factor binding in GM12878 cell line, from ENCODE database)

generateWig( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, span=200, capping=0, normConst=1 )

constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binTFBS <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binTFBS
head(print(binTFBS))
plot(binTFBS)
plot( binTFBS, plotType="input" )

fitTFBS <- mosaicsFit( binTFBS, analysisType="IO", bgEst="rMOM" )
fitTFBS
plot(fitTFBS)

peakTFBS <- mosaicsPeak( fitTFBS, signalModel="2S", FDR=0.05,
maxgap=200, minsize=50, thres=10 )
peakTFBS
head(print(peakTFBS))

peakTFBS <- extractReads( peakTFBS,
  chipFile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam"), package="mosaics",
  chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam"), package="mosaics",
  controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakTFBS

peakTFBS <- findSummit( peakTFBS, parallel=FALSE, nCore=8 )

export( peakTFBS, type = "txt", filename = "./peakTFBS.txt" )
export( peakTFBS, type = "bed", filename = "./peakTFBS.bed" )
export( peakTFBS, type = "gff", filename = "./peakTFBS.gff" )
export( peakTFBS, type = "narrowPeak", filename = "./peakTFBS.narrowPeak" )

# example analysis workflow for ChIP-seq data of histone modification
# (H3K4me3 modification in GM12878 cell line, from ENCODE database)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

```

```

byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
PET=FALSE, fragLen=200, binSize=200, capping=0 )

fileName <- file.path(
  c("wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
    "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt"))
binHM <- readBins( type=c("chip", "input"), fileName=fileName )
binHM
plot(binHM)
plot( binHM, plotType="input" )

fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
fitHM
plot(fitHM)

hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
hmmHM
plot(hmmHM)

peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), pa
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam")
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
head(print(peakHM))
plot( peakHM, filename=".~/peakplot_HM.pdf" )

peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

export( peakHM, type = "txt", filename = ".~/peakHM.txt" )
export( peakHM, type = "bed", filename = ".~/peakHM.bed" )
export( peakHM, type = "gff", filename = ".~/peakHM.gff" )
export( peakHM, type = "narrowPeak", filename = ".~/peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = ".~/peakHM.broadPeak" )

## End(Not run)

```

Description

Adjust boundaries of peak regions in the `MosaicsPeak` class object, which is a peak calling result.

Usage

```
adjustBoundary( object, ... )
## S4 method for signature 'MosaicsPeak'
adjustBoundary( object, minRead=10, extendFromSummit=100,
  trimMinRead1=1.5, trimFC1=5, extendMinRead1=2, extendFC1=50,
  trimMinRead2=1.5, trimFC2=50, extendMinRead2=1.5, extendFC2=50,
  normC=NA, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|-------------------------------|--|
| <code>object</code> | Object of class <code>MosaicsPeak</code> , a peak list object obtained using either functions <code>mosaicsPeak</code> or <code>mosaicsPeakHMM</code> . |
| <code>minRead</code> | Parameter to determine baseline for trimming and extension of peak boundaries. |
| <code>extendFromSummit</code> | If the updated peak regions do not include the peak summit, either peak start or end is extended by <code>extendFromSummit</code> . |
| <code>trimMinRead1</code> | Parameter to determine to trim peak boundaries. |
| <code>trimFC1</code> | Parameter to determine to trim peak boundaries. |
| <code>extendMinRead1</code> | Parameter to determine to extend peak boundaries. |
| <code>extendFC1</code> | Parameter to determine to extend peak boundaries. |
| <code>trimMinRead2</code> | Parameter used to trim peak boundaries. |
| <code>trimFC2</code> | Parameter used to trim peak boundaries. |
| <code>extendMinRead2</code> | Parameter used to extend peak boundaries. |
| <code>extendFC2</code> | Parameter used to extend peak boundaries. |
| <code>normC</code> | Normalizing constant. If not provided, <code>normC</code> is estimated as ratio of sequencing depth of ChIP over matched control samples. |
| <code>parallel</code> | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are <code>TRUE</code> (utilize multiple CPUs) or <code>FALSE</code> (do not utilize multiple CPUs). Default is <code>FALSE</code> (do not utilize multiple CPUs). |
| <code>nCore</code> | Number of CPUs when parallel computing is utilized. |
| <code>...</code> | Other parameters to be passed through to generic <code>mosaicsHMM</code> . |

Details

`adjustBoundary` adjusts peak boundaries. While `adjustBoundary` can be applied to a peak list object obtained using either functions `mosaicsPeak` or `mosaicsPeakHMM`, `adjustBoundary` is developed and tested mainly for peak lists from MOSAiCS-HMM model (i.e., from function `mosaicsPeakHMM`). Note that `extractReads` should be run first because `adjustBoundary` is used.

Parallel computing can be utilized for faster computing if `parallel=TRUE` and `parallel` package is loaded. `nCore` determines number of CPUs used for parallel computing.

Value

Construct MosaicsPeak class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [extractReads](#), [findSummit](#), [filterPeak](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=".",
  byChr=FALSE, useChrfile=FALSE, chrfi

```

```
## End(Not run)
```

BinData-class

Class "BinData"

Description

This class represents bin-level ChIP-seq data.

Objects from the Class

Objects can be created by calls of the form `new("BinData", ...)`.

Slots

chrID: Object of class "character", a vector of chromosome IDs.
coord: Object of class "numeric", a vector of genomic coordinates.
tagCount: Object of class "numeric", a vector of tag counts of ChIP sample.
mappability: Object of class "numeric", a vector of mappability score.
gcContent: Object of class "numeric", a vector of GC content score.
input: Object of class "numeric", a vector of tag counts of matched control sample.
dataType: Object of class "character", indicating how reads were processed. Possible values are "unique" (only uniquely aligned reads were retained) and "multi" (reads aligned to multiple locations were also retained).
seqDepth: Object of class "numeric", a vector of sequencing depth of length 2, where the first and second elements correpond to sequencing depths of ChIP and control samples, respectively. If there is not control sample, the second element is set to NA.

Methods

mosaicsFit `signature(object = "BinData")`: fit a MOSAiCS model using a bin-level ChIP-seq data.

plot `signature(x = "BinData", y = "missing", plotType = NULL)`: provide exploratory plots of mean ChIP tag counts. This method plots mean ChIP tag counts versus mappability score, GC content score, and Control tag counts, with 95% confidence intervals, for `plotType="M"`, `plotType="GC"`, and `plotType="input"`, respectively. `plotType="M|input"` and `plotType="GC|input"` provide plots of mean ChIP tag counts versus mappability and GC content score, respectively, conditional on Control tag counts. If `plotType` is not specified, this method plots histogram of ChIP tag counts.

print `signature(x = "BinData")`: return bin-level data in data frame format.

show `signature(object = "BinData")`: provide brief summary of the object.

chrID `signature(object = "BinData")`: provide a vector of chromosome ID.

coord `signature(object = "BinData")`: provide a vector of genomic coordinates.

tagCount signature(object = "BinData"): provide a vector of tag count of ChIP sample.

input signature(object = "BinData"): provide a vector of tag count of input sample.

mappability signature(object = "BinData"): provide a vector of mappability score.

gcContent signature(object = "BinData"): provide a vector of GC content score.

seqDepth signature(object = "BinData"): provide a vector of sequencing depth.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[readBins](#), [mosaicsFit](#).

Examples

```
showClass("BinData")
## Not run:
library(mosaicsExample)
data(exampleBinData)

exampleBinData
print(exampleBinData)[1:10,]
plot(exampleBinData)
plot( exampleBinData, plotType="M" )
plot( exampleBinData, plotType="GC" )
plot( exampleBinData, plotType="input" )
plot( exampleBinData, plotType="M|input" )
plot( exampleBinData, plotType="GC|input" )

exampleFit <- mosaicsFit( exampleBinData, analysisType="IO" )

## End(Not run)
```

constructBins*Construct bin-level ChIP-sep data from an aligned read file*

Description

Preprocess and construct bin-level ChIP-sep data from an aligned read file.

Usage

```
constructBins( infile=NULL, fileFormat=NULL, outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0, perl = "perl" )
```

Arguments

| | |
|------------|--|
| infile | Name of the aligned read file to be processed. |
| fileFormat | Format of the aligned read file to be processed. Currently, constructBins permits the following aligned read file formats for SET data (PET = FALSE): "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bam" (BAM), "bed" (BED), and "csem" (CSEM). For PET data (PET = TRUE), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM). |
| outfileLoc | Directory of processed bin-level files. By default, processed bin-level files are exported to the current directory. |
| byChr | Construct separate bin-level file for each chromosome? Possible values are TRUE or FALSE. If byChr=FALSE, bin-level data for all chromosomes are exported to one file. If byChr=TRUE, bin-level data for each chromosome is exported to a separate file. Default is FALSE. |
| useChrfile | Is the file for chromosome info provided? Possible values are TRUE or FALSE. If useChrfile=FALSE, it is assumed that the file for chromosome info is not provided. If useChrfile=TRUE, it is assumed that the file for chromosome info is provided. Default is FALSE. |
| chrfile | Name of the file for chromosome info. In this file, the first and second columns are ID and size of each chromosome, respectively. |
| excludeChr | Vector of chromosomes that will be excluded from the analysis. This argument is ignored if useChrfile=TRUE. |
| PET | Is the file paired-end tag (PET) data? If PET=FALSE, it is assumed that the file is SET data. If PET=TRUE, it is assumed that the file is PET data. Default is FALSE (SET data). |
| fragLen | Average fragment length. Default is 200. This argument is ignored if PET=TRUE. |
| binSize | Size of bins. Default is 200. |

| | |
|---------|--|
| capping | Maximum number of reads allowed to start at each nucleotide position. To avoid potential PCR amplification artifacts, the maximum number of reads that can start at a nucleotide position is capped at capping. Capping is not applied if non-positive value is used for capping. Default is 0 (no capping). |
| perl | Name of the perl executable to be called. Default is "perl". |

Details

Bin-level files are constructed from the aligned read file and exported to the directory specified in `outfileLoc` argument. If `byChr=FALSE`, bin-level files are named as `[infFileName]_fragL[fragLen]_bin[binSize].txt` for SET data (PET = FALSE) and `[infFileName]_bin[binSize].txt` for PET data (PET = TRUE). If `byChr=TRUE`, bin-level files are named as `[infFileName]_fragL[fragLen]_bin[binSize]_[chrID].txt` for SET data (PET = FALSE) and `[infFileName]_bin[binSize]_[chrID].txt` for PET data (PET = TRUE), where `chrID` is chromosome IDs that reads align to. These chromosome IDs are extracted from the aligned read file.

If the file for chromosome information is provided (`useChrfile=TRUE` and `chrfile` is not NULL), only the chromosomes specified in the file will be considered. Chromosomes that are specified in `excludeChr` will not be included in the processed bin-level files. `excludeChr` argument is ignored if `useChrfile=TRUE`. Constructed bin-level files can be loaded into the R environment using the method `readBins`.

`constructBins` currently supports the following aligned read file formats for SET data (PET = FALSE): Eland result ("eland_result"), Eland extended ("eland_extended"), Eland export ("eland_export"), default Bowtie ("bowtie"), SAM ("sam"), "bam" (BAM), BED ("bed"), and CSEM ("csem"). For PET data (PET = TRUE), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM).

If input file format is neither BED nor CSEM BED, this method retains only reads mapping uniquely to the reference genome.

Value

Processed bin-level files are exported to the directory specified in `outfileLoc`.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[readBins](#), [BinData](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc= "./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc= "./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binHM

## End(Not run)
```

estimates

Extract estimates of the fitted MOSAiCS model

Description

Extract estimates from `MosaicsFit` class object, which is a fitted MOSAiCS model.

Usage

```
estimates( object, ... )
## S4 method for signature 'MosaicsFit'
estimates( object )
```

Arguments

`object` Object of class `MosaicsFit`, which represents a fitted MOSAiCS model obtained using method `mosaicsFit`.
`...` Other parameters to be passed through to generic `estimates`.

Value

Returns a list with components:

| | |
|----------------------|---|
| <code>pi0</code> | Mixing proportion of background component. |
| <code>a</code> | Parameter for background component. |
| <code>betaEst</code> | Parameter for background component (coefficient estimates). |
| <code>muEst</code> | Parameter for background component. |

| | |
|--------------|--|
| b | Parameter for one-signal-component model. |
| c | Parameter for one-signal-component model. |
| p1 | Parameter for two-signal-component model (mixing proportion of signal components). |
| b1 | Parameter for two-signal-component model (the first signal component). |
| c1 | Parameter for two-signal-component model (the first signal component). |
| b2 | Parameter for two-signal-component model (the second signal component). |
| c2 | Parameter for two-signal-component model (the second signal component). |
| analysisType | Analysis type. Possible values are "OS" (one-sample analysis), "TS" (two-sample analysis using mappability and GC content), and "IO" (two-sample analysis without using mappability and GC content). |

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFit](#), [MosaicsFit](#).

Examples

```
## Not run:
library(mosaicsExample)
data(exampleBinData)
exampleFit <- mosaicsFit( exampleBinData, analysisType="IO" )
estimates(exampleFit)

## End(Not run)
```

| | |
|--------|--|
| export | <i>Export peak calling results to text files</i> |
|--------|--|

Description

Export peak calling results to text files in TXT, BED, or GFF file formats.

Usage

```
export(object, ...)
## S4 method for signature 'MosaicsPeak'
export( object, type=NA, filename=NA )
```

Arguments

| | |
|----------|---|
| object | Object of class <code>MosaicsPeak</code> , peak calling results obtained using method <code>mosaicsPeak</code> . |
| type | Format of the exported file. Possible values are "txt", "bed", "gff", "narrowPeak", and "broadPeak". See Details. |
| filename | Name of the exported file. |
| ... | Other parameters to be passed through to generic <code>export</code> . |

Details

TXT file format (type="txt") exports peak calling results in the most informative way. Columns include chromosome ID, peak start position, peak end position, peak width, -log10 transformed average posterior probability, -log10 transformed minimum posterior probability, average of -log10 transformed posterior probability, average ChIP tag count, maximum ChIP tag count (always), average input tag count, average input tag count scaled by sequencing depth, average log base 2 ratio of ChIP over input tag counts (if matched control sample is also provided), average mappability score, and average GC content score (when mappability and GC content scores are used in the analysis) in each peak. type="bed" and type="gff" export peak calling results in standard BED and GFF file formats, respectively, where score is the average ChIP tag counts in each peak. type="narrowPeak" and type="broadPeak" export peak calling results in ENCODE narrowPeak and broadPeak file formats, respectively, where score, signalValue, pValue, and qValue are average log base 2 ratio of ChIP over input tag counts (or average ChIP tag count, if matched control sample is not provided), ChIP signal at the summit, -log10 transformation of minimum posterior probability (logMinP), and average of -log10 transformed posterior probability (aveLogP), respectively, in each peak. If no peak is detected, `export` method will not generate any file.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

export( peakHM, type = "txt", filename = "./peakHM.txt" )
export( peakHM, type = "bed", filename = "./peakHM.bed" )
export( peakHM, type = "gff", filename = "./peakHM.gff" )

# read-level data is needed to loaded and peak summits need to be identified
# to export in narrowPeak and broadPeak file formats

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), path="bed",
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"), path="bed",
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
```

```

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
export( peakHM, type = "narrowPeak", filename = "./peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = "./peakHM.broadPeak" )

## End(Not run)

```

extractReads

Load read-level data and extract reads corresponding to each peak region

Description

Load read-level data and extract reads corresponding to each peak region in the `MosaicsPeak` class object, which is a peak calling result.

Usage

```

extractReads( object, ... )
## S4 method for signature 'MosaicsPeak'
extractReads( object, chipFile=NULL, chipFileFormat=NULL,
  chipPET=FALSE, chipFragLen=200,
  controlFile=NULL, controlFileFormat=NULL,
  controlPET=FALSE, controlFragLen=200, keepReads=FALSE,
  parallel=FALSE, nCore=8, tempDir=NULL, perl="perl" )

```

Arguments

| | |
|-----------------------------|---|
| <code>object</code> | Object of class <code>MosaicsPeak</code> , a peak list object obtained using either functions <code>mosaicsPeak</code> or <code>mosaicsPeakHMM</code> . |
| <code>chipFile</code> | Name of the aligned read file for ChIP sample. |
| <code>chipFileFormat</code> | Format of the aligned read file for ChIP sample. Currently, <code>constructBins</code> permits the following aligned read file formats for SET data (<code>chipPET</code> = FALSE): "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bam" (BAM), "bed" (BED), and "csem" (CSEM). For PET data (<code>chipPET</code> = TRUE), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM). |
| <code>chipPET</code> | Is the file of ChIP sample paired-end tag (PET) data? If <code>chipPET</code> =FALSE, it is assumed that the file is SET data. If <code>chipPET</code> =TRUE, it is assumed that the file is PET data. Default is FALSE (SET data). |
| <code>chipFragLen</code> | Average fragment length of ChIP sample. Default is 200. This argument is ignored if <code>chipPET</code> =TRUE. |
| <code>controlFile</code> | Name of the aligned read file for matched control sample. |

| | |
|--------------------------------|--|
| <code>controlFileFormat</code> | Format of the aligned read file for matched control sample. Currently, <code>constructBins</code> permits the following aligned read file formats for SET data (<code>controlPET = FALSE</code>): "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bam" (BAM), "bed" (BED), and "csem" (CSEM). For PET data (<code>controlPET = TRUE</code>), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM). |
| <code>controlPET</code> | Is the file of matched control sample paired-end tag (PET) data? If <code>controlPET=FALSE</code> , it is assumed that the file is SET data. If <code>controlPET=TRUE</code> , it is assumed that the file is PET data. Default is FALSE (SET data). |
| <code>controlFragLen</code> | Average fragment length of matched control sample. Default is 200. This argument is ignored if <code>controlPET=TRUE</code> . |
| <code>keepReads</code> | Keep read-level data? Default is FALSE (do not keep read-level data). |
| <code>parallel</code> | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (utilize multiple CPUs) or FALSE (do not utilize multiple CPUs). Default is FALSE (do not utilize multiple CPUs). |
| <code>nCore</code> | Number of CPUs when parallel computing is utilized. |
| <code>tempDir</code> | Directory to store temporary files. If <code>tempDir=NULL</code> , <code>extractReads()</code> will use the temporary directory used by R. |
| <code>perl</code> | Name of the perl executable to be called. Default is "perl". |
| ... | Other parameters to be passed through to generic <code>extractReads</code> . |

Details

Read-level data is first loaded from aligned read files, and then the reads corresponding to each peak region are extracted and incorporated into the `MosaicsPeak` class object. `extractReads` currently supports the following aligned read file formats for SET data (`chipPET = FALSE` and `controlPET = FALSE`): Eland result ("eland_result"), Eland extended ("eland_extended"), Eland export ("eland_export"), default Bowtie ("bowtie"), SAM ("sam"), BAM ("bam"), BED ("bed"), and CSEM ("csem"). For PET data (`chipPET = FALSE` and `controlPET = FALSE`), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM).

If input file format is neither BED nor CSEM BED, this method retains only reads mapping uniquely to the reference genome.

Value

Construct `MosaicsPeak` class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [export](#), [findSummit](#), [adjustBoundary](#), [filterPeak](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=". /",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=". /",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"),
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"),
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )

## End(Not run)
```

| | |
|------------|--|
| filterPeak | <i>Filter out potentially false positive peaks</i> |
|------------|--|

Description

Filter out potentially false positive peaks from `MosaicsPeak` class object, which is a peak calling result.

Usage

```
filterPeak( object, ... )
## S4 method for signature 'MosaicsPeak'
filterPeak( object,
  minSummitQuantile=0.01, minRead=10, FC=50, minSignal = 20, minLen = 200,
  normC=NA, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|--------------------------------|--|
| <code>object</code> | Object of class <code>MosaicsPeak</code> , a peak list object obtained using either functions <code>mosaicsPeak</code> or <code>mosaicsPeakHMM</code> . |
| <code>minSummitQuantile</code> | Parameter for the filtering step #1. Peaks are filtered out if signal strengths at summits < <code>minSummitQuantile</code> quantile of signal strengths at summits across all the peak regions. |
| <code>minRead</code> | Parameter for the filtering step #1. Peaks are filtered out if the number of reads in the peak region < <code>minRead</code> . |
| <code>FC</code> | Parameter for the filtering step #1. Peaks are filtered out if the improvement of ChIP over matched control < <code>FC</code> . |
| <code>minSignal</code> | Parameter for the filtering step #2. Peaks are filtered out if signal strengths at summits <= <code>minSignal</code> . |
| <code>minLen</code> | Parameter for the filtering step #2. Peaks are filtered out if their lengths <= <code>minLen</code> . |
| <code>normC</code> | Normalizing constant. If not provided, <code>normC</code> is estimated as ratio of sequencing depth of ChIP over matched control samples. |
| <code>parallel</code> | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are <code>TRUE</code> (utilize multiple CPUs) or <code>FALSE</code> (do not utilize multiple CPUs). Default is <code>FALSE</code> (do not utilize multiple CPUs). |
| <code>nCore</code> | Number of CPUs when parallel computing is utilized. |
| ... | Other parameters to be passed through to generic <code>filterPeak</code> . |

Details

`filterPeak` filters out potentially false positive peaks, based on signal strengths and peak lengths. While `filterPeak` can be applied to a peak list object obtained using either functions `mosaicsPeak` or `mosaicsPeakHMM`, `filterPeak` is developed and tested mainly for peak lists from MOSAiCS-HMM model (i.e., from function `mosaicsPeakHMM`). Note that `extractReads` should be run first because `filterPeak` is used.

Value

Construct MosaicsPeak class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [extractReads](#), [findSummit](#), [adjustBoundary](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=".",
  byChr=FALSE, useChrfile=FALSE, chrfi

```

```
## End(Not run)
```

findSummit*Find a summit for each peak region*

Description

Find a summit for each peak region in the `MosaicsPeak` class object, which is a peak calling result.

Usage

```
findSummit( object, ... )
## S4 method for signature 'MosaicsPeak'
findSummit( object, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|----------|---|
| object | Object of class <code>MosaicsPeak</code> , a peak list object obtained using either functions <code>mosaicsPeak</code> or <code>mosaicsPeakHMM</code> . |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (utilize multiple CPUs) or FALSE (do not utilize multiple CPUs). Default is FALSE (do not utilize multiple CPUs). |
| nCore | Number of CPUs when parallel computing is utilized. |
| ... | Other parameters to be passed through to generic <code>findSummit</code> . |

Details

Note that `extractReads` should be run first because `findSummit` is used.

Value

Construct `MosaicsPeak` class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [export](#), [extractReads](#), [adjustBoundary](#), [filterPeak](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfi=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfi=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), package="mosaicsExample"),
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"), package="mosaicsExample"),
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )

export( peakHM, type = "narrowPeak", filename = "./peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = "./peakHM.broadPeak" )

## End(Not run)
```

generateWig

Construct wiggle files from an aligned ChIP-sep read file

Description

Construct wiggle files from an aligned ChIP-sep read file.

Usage

```
generateWig( infile=NULL, fileFormat=NULL, outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, span=200, capping=0, normConst=1, perl = "perl" )
```

Arguments

| | |
|------------|--|
| infile | Name of the aligned read file to be processed. |
| fileFormat | Format of the aligned read file to be processed. Currently, generateWig permits the following aligned read file formats for SET data (PET = FALSE): "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bam" (BAM), "bed" (BED), and "csem" (CSEM). For PET data (PET = TRUE), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM). |
| outfileLoc | Directory of processed wiggle files. By default, processed wiggle files are exported to the current directory. |
| byChr | Construct separate wiggle file for each chromosome? Possible values are TRUE or FALSE. If byChr=FALSE, all chromosomes are exported to one file. If byChr=TRUE, each chromosome is exported to a separate file. Default is FALSE. |
| useChrfile | Is the file for chromosome info provided? Possible values are TRUE or FALSE. If useChrfile=FALSE, it is assumed that the file for chromosome info is not provided. If useChrfile=TRUE, it is assumed that the file for chromosome info is provided. Default is FALSE. |
| chrfile | Name of the file for chromosome info. In this file, the first and second columns are ID and size of each chromosome, respectively. |
| excludeChr | Vector of chromosomes that will be excluded from the analysis. This argument is ignored if useChrfile=TRUE. |
| PET | Is the file paired-end tag (PET) data? If PET=FALSE, it is assumed that the file is SET data. If PET=TRUE, it is assumed that the file is PET data. Default is FALSE (SET data). |
| fragLen | Average fragment length. Default is 200. This argument is ignored if PET=TRUE. |
| span | Span used in wiggle files. Default is 200. |
| capping | Maximum number of reads allowed to start at each nucleotide position. To avoid potential PCR amplification artifacts, the maximum number of reads that can start at a nucleotide position is capped at capping. Capping is not applied if non-positive value is used for capping. Default is 0 (no capping). |
| normConst | Normalizing constant to scale values in each position. |
| perl | Name of the perl executable to be called. Default is "perl". |

Details

Wiggle files are constructed from the aligned read file and exported to the directory specified in outfileLoc argument. If byChr=FALSE, wiggle files are named as [infileName]_fragL[fragLen]_span[span].wig for SET data (PET = FALSE) and [infileName]_span[span].wig for PET data (PET = TRUE). If

byChr=TRUE, wiggle files are named as [infelName]_fragL[fragLen]_span[span]_[chrID].wig for SET data (PET = FALSE) and [infelName]_span[span]_[chrID].wig for PET data (PET = TRUE), where chrID is chromosome IDs that reads align to. These chromosome IDs are extracted from the aligned read file.

If the file for chromosome information is provided (useChrfile=TRUE and chrfile is not NULL), only the chromosomes specified in the file will be considered. Chromosomes that are specified in excludeChr will not be included in the processed wiggle files. excludeChr argument is ignored if useChrfile=TRUE.

generateWig currently supports the following aligned read file formats for SET data (PET = FALSE): Eland result ("eland_result"), Eland extended ("eland_extended"), Eland export ("eland_export"), default Bowtie ("bowtie"), SAM ("sam"), , "bam" (BAM), BED ("bed"), and CSEM ("csem"). For PET data (PET = TRUE), the following aligned read file formats are allowed: "eland_result" (Eland result), "sam" (SAM), and "bam" (BAM).

If input file format is neither BED nor CSEM BED, this method retains only reads mapping uniquely to the reference genome.

Value

Processed wig files are exported to the directory specified in outfileLoc.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

Examples

```
## Not run:
library(mosaicsExample)

generateWig( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAlnRep1_chr22_sorted.bam")
  fileFormat="bam", outfileLoc=".",
  PET=FALSE, fragLen=200, span=200, capping=0, normConst=1 )

## End(Not run)
```

| | |
|------------------|---------------------------------|
| mosaics-internal | <i>Internal mosaics objects</i> |
|------------------|---------------------------------|

Description

Internal mosaics objects.

Details

These are not to be called by the user.

| | |
|------------|--------------------------|
| mosaicsFit | <i>Fit MOSAiCS model</i> |
|------------|--------------------------|

Description

Fit one-sample or two-sample MOSAiCS models with one signal component and two signal components.

Usage

```
mosaicsFit( object, ... )
## S4 method for signature 'BinData'
mosaicsFit( object, analysisType="automatic", bgEst="rMOM",
            k=3, meanThres=NA, s=2, d=0.25, trans="power", truncProb=0.999, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|--------------|---|
| object | Object of class <code>BinData</code> , bin-level ChIP-seq data imported using method <code>readBins</code> . |
| analysisType | Analysis type. Possible values are "OS" (one-sample analysis), "TS" (two-sample analysis using mappability and GC content), and "IO" (two-sample analysis without using mappability and GC content). If <code>analysisType="automatic"</code> , this method tries to make the best guess for <code>analysisType</code> , based on the data provided. |
| bgEst | Parameter to determine background estimation approach. Possible values are "matchLow" (estimation using bins with low tag counts) and "rMOM" (estimation using robust method of moment (MOM)). If <code>bgEst="automatic"</code> , this method tries to make the best guess for <code>bgEst</code> , based on the data provided. Default is <code>bgEst="rMOM"</code> . |
| k | Parameter for estimating background distribution. It is not recommended for users to change this value. |
| meanThres | Parameter for estimating background distribution. Default is 1 for <code>analysisType="TS"</code> and 0 for <code>analysisType="OS"</code> . Not relevant when <code>analysisType="IO"</code> . |

| | |
|-----------|---|
| s | Parameter for estimating background distribution. Relevant only when analysisType="TS". Default is 2. |
| d | Parameter for estimating background distribution. Relevant only when analysisType="TS" or analysisType="IO". Default is 0.25. |
| trans | Transformation of matching control tag count. Possible values are "log" (logarithm transformation) and "power" (power transformation). Relevant only when analysisType="IO". Default is trans="power". |
| truncProb | Parameter for estimating background distribution. Relevant only when analysisType="IO". |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (utilize multiple CPUs) or FALSE (do not utilize multiple CPUs). Default is FALSE (do not utilize multiple CPUs). |
| nCore | Number of CPUs when parallel computing is utilized. |
| ... | Other parameters to be passed through to generic mosaicsFit. |

Details

The imported data type constraints the analysis that can be implemented. If only data for ChIP sample and matched control sample (i.e., either type=c("chip", "input") or type=c("chip", "input", "N") was used in method `readBins`), only two-sample analysis without using mappability and GC content (analysisType="IO") is allowed. If matched control data is available with mappability score, GC content score, and sequence ambiguity score, (i.e., type=c("chip", "input", "M", "GC", "N") was used in method `readBins`), user can do all of three analysis types (analysisType="OS", analysisType="TS", or analysisType="IO"). If there is no data for matched control sample (i.e., type=c("chip", "M", "GC", "N") was used in method `readBins`), only one-sample analysis (analysisType="OS") is permitted.

Parallel computing can be utilized for faster computing if `parallel`=TRUE and `parallel` package is loaded. `nCore` determines number of CPUs used for parallel computing. `meanThres`, `s`, `d`, `trans`, and `truncProb` are the tuning parameters for estimating background distribution. The vignette and Kuan et al. (2011) provide further details about these tuning parameters. Please do not try different value for `k` argument.

Value

Construct `MosaicsFit` class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[readBins](#), [mosaicsFitHMM](#), [MosaicsFit](#).

Examples

```
## Not run:
library(mosaicsExample)
data(exampleBinData)
exampleFit <- mosaicsFit( exampleBinData, analysisType="IO" )

## End(Not run)
```

Description

This class represents MOSAiCS model fit.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsFit", ...)`.

Slots

mosaicsEst: Object of class "MosaicsFitEst", representing estimates of MOSAiCS model fit.

mosaicsParam: Object of class "MosaicsFitParam", representing tuning parameters for fitting MOSAiCS model.

chrID: Object of class "character", a vector of chromosome IDs.

coord: Object of class "numeric", a vector of genomic coordinates.

tagCount: Object of class "numeric", a vector of tag counts of ChIP sample.

mappability: Object of class "numeric", a vector of mappability score.

gcContent: Object of class "numeric", a vector of GC content score.

input: Object of class "numeric", a vector of tag counts of matched control sample.

bic1S: Object of class "numeric", Bayesian Information Criterion (BIC) value of one-signal-component model.

bic2S: Object of class "numeric", Bayesian Information Criterion (BIC) value of two-signal-component model.

seqDepth: Object of class "numeric", a vector of sequencing depth of length 2, where the first and second elements correpond to sequencing depths of ChIP and control samples, respectively. If there is not control sample, the second element is set to NA.

Methods

```

estimates signature(object = "MosaicsFit"): extract estimates from MOSAiCS model fit.

mosaicsPeak signature(object = "MosaicsFit"): call peaks using MOSAiCS model fit.

plot signature(x = "MosaicsFit", y = "missing"): draw Goodness of Fit (GOF) plot.

print signature(x = "MosaicsFit"): (not supported yet)

show signature(object = "MosaicsFit"): provide brief summary of the object.

seqDepth signature(object = "MosaicsFit"): provide a vector of sequencing depth.

```

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFit](#), [mosaicsPeak](#), [mosaicsFitHMM](#), [estimates](#).

Examples

```

showClass("MosaicsFit")
## Not run:
library(mosaicsExample)

data(exampleBinData)
exampleFit <- mosaicsFit( exampleBinData, analysisType="IO" )

exampleFit
plot(exampleFit)
estimates(exampleFit)

examplePeak <- mosaicsPeak( exampleFit, signalModel = "2S", FDR = 0.05 )

## End(Not run)

```

MosaicsFitEst-class *Class "MosaicsFitEst"*

Description

This class represents estimates of mosaicsFit function.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsFitEst", ...)`.

Slots

pi0: Object of class "numeric", representing mixing proportion of background component.

a: Object of class "numeric", representing parameter for background component.

betaEst: Object of class "numeric", representing parameter for background component (coefficient estimates).

muEst: Object of class "numeric", representing parameter for background component.

pNfit: Object of class "list", representing background model fit.

b: Object of class "numeric", representing parameter for one-signal-component model.

c: Object of class "numeric", representing parameter for one-signal-component model.

p1: Object of class "numeric", representing parameter for two-signal-component model (mixing proportion of signal components).

b1: Object of class "numeric", representing parameter for two-signal-component model (the first signal component).

c1: Object of class "numeric", representing parameter for two-signal-component model (the first signal component).

b2: Object of class "numeric", representing parameter for two-signal-component model (the second signal component).

c2: Object of class "numeric", representing parameter for two-signal-component model (the second signal component).

inputTrunc: Object of class "numeric", representing parameter for input-only analysis (threshold for maximum tag count for matched control sample).

analysisType: Object of class "character", representing type of data analysis.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFit](#).

Examples

```
showClass("MosaicsFitEst")
```

mosaicsFitHMM

Fit MOSAiCS-HMM model

Description

Fit MOSAiCS-HMM model.

Usage

```
mosaicsFitHMM( object, ... )
## S4 method for signature 'MosaicsFit'
mosaicsFitHMM( object, signalModel="2S", binsize=NA,
  init="mosaics", init.FDR=0.05,
  init.maxgap=200, init.minsize=50, init.thres=10, init.piMat=as.matrix(NA),
  max.iter=100, eps=1e-20, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|-------------|--|
| object | Object of class <code>MosaicsFit</code> , a fitted MOSAiCS model obtained using function <code>mosaicsFit</code> . |
| signalModel | Signal model. Possible values are "1S" (one-signal-component model) and "2S" (two-signal-component model). Default is "2S". |
| binsize | Size of each bin. Value should be positive integer. If <code>binsize=NA</code> , <code>mosaicsFitHMM</code> function calculates the value from data. Default is NA. |
| init | Approach to initialize MOSAiCS-HMM. Possible values are "mosaics" (use MOSAiCS peak calling results for initialization) or "specify" (explicitly specify transition matrix). Default is "mosaics". |
| init.FDR | Parameter for the MOSAiCS-HMM initialization. False discovery rate. Default is 0.05. Related only if <code>init="mosaics"</code> . |

| | |
|--------------|--|
| init.maxgap | Parameter for the MOSAiCS-HMM initialization. Initial nearby peaks are merged if the distance (in bp) between them is less than init.maxgap. Default is 200. Related only if init="mosaics". |
| init.minsize | Parameter for the MOSAiCS-HMM initialization. An initial peak is removed if its width is narrower than init.minsize. Default is 50. Related only if init="mosaics". |
| init.thres | Parameter for the MOSAiCS-HMM initialization. A bin within initial peak is removed if its ChIP tag counts are less than init.thres. Default is 10. Related only if init="mosaics". |
| init.piMat | Initial value for transition matrix. The first rows/columns correspond to the non-binding state while the second rows/columns correspond to the binding state. Related only if init="specify". If init="specify" but init.piMat is not specified, mosaicsFitHMM() uses its default for the MOSAiCS-HMM initialization. |
| max. iter | Number of iterations for fitting MOSAiCS-HMM. Default is 100. |
| eps | Criterion to stop iterations for fitting MOSAiCS-HMM. Default is 1e-20. |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (utilize multiple CPUs) or FALSE (do not utilize multiple CPUs). Default is FALSE (do not utilize multiple CPUs). |
| nCore | Number of CPUs when parallel computing is utilized. |
| ... | Other parameters to be passed through to generic mosaicsFitHMM. |

Details

mosaicsFitHMM and mosaicsPeakHMM are developed to identify broad peaks such as histone modifications, using Hidden Markov Model (HMM) approach, as proposed in Chung et al. (2014). If you are interested in identifying narrow peaks such as transcription factor binding sites, please use mosaicsPeak instead of mosaicsFitHMM and mosaicsPeakHMM.

When peaks are called, proper signal model needs to be specified. The optimal choice for the number of signal components depends on the characteristics of ChIP-seq data. In order to support users in the choice of optimal signal model, Bayesian Information Criterion (BIC) values and Goodness of Fit (GOF) plot are provided for the fitted MOSAiCS model. BIC values and GOF plot can be obtained by applying show and plot methods, respectively, to the MosaicsFit class object, which is a fitted MOSAiCS model.

init.FDR, init.maxgap, init.minsize, and init.thres are the parameters for MOSAiCS-HMM initialization when MOSAiCS peak calling results are used for initialization (init="mosaics"). If user specifies transition matrix (init="specify"), only init.piMat is used for initialization. If you use a bin size shorter than the average fragment length of the experiment, we recommend to set init.maxgap to the average fragment length and init.minsize to the bin size. If you set the bin size to the average fragment length or if bin size is larger than the average fragment length, set init.maxgap to the average fragment length and init.minsize to a value smaller than the average fragment length. See the vignette for further details.

Parallel computing can be utilized for faster computing if parallel=TRUE and parallel package is loaded. nCore determines number of CPUs used for parallel computing.

Value

Construct MosaicsHMM class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

`mosaicsFit`, `mosaicsPeakHMM`, `MosaicsFit`, `MosaicsHMM`.

Examples

```

## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binHM
plot(binHM)
plot( binHM, plotType="input" )

fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
fitHM
plot(fitHM)

hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
hmmHM
plot(hmmHM)

peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  nCore=8 )

```

```

thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), pa
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam")
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
head(print(peakHM))
plot( peakHM, filename="./peakplot_HM.pdf" )

peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

export( peakHM, type = "txt", filename = "./peakHM.txt" )
export( peakHM, type = "bed", filename = "./peakHM.bed" )
export( peakHM, type = "gff", filename = "./peakHM.gff" )
export( peakHM, type = "narrowPeak", filename = "./peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = "./peakHM.broadPeak" )

## End(Not run)

```

MosaicsFitParam-class *Class "MosaicsFitParam"*

Description

This class represents parameters for mosaicsFit function.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsFitParam", ...)`.

Slots

- k:** Object of class "numeric", representing a parameter for mosaicsFit function.
- meanThres:** Object of class "numeric", representing a parameter for mosaicsFit function.
- s:** Object of class "numeric", representing a parameter for mosaicsFit function.
- d:** Object of class "numeric", representing a parameter for mosaicsFit function.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFit](#).

Examples

```
showClass("MosaicsFitParam")
```

| | |
|------------------|--------------------|
| MosaicsHMM-class | Class "MosaicsHMM" |
|------------------|--------------------|

Description

This class represents MOSAiCS-HMM model fit.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsHMM", ...)`.

Slots

- HMfit:** Object of class "list", representing the fitted MOSAiCS-HMM model.
- chrID:** Object of class "character", a vector of chromosome IDs.
- coord:** Object of class "numeric", a vector of genomic coordinates.
- tagCount:** Object of class "numeric", a vector of tag counts of ChIP sample.
- mappability:** Object of class "numeric", a vector of mappability score.
- gcContent:** Object of class "numeric", a vector of GC content score.
- input:** Object of class "numeric", a vector of tag counts of matched control sample.
- inputdata:** Object of class "list", representing the bin-level data.
- mosaicsEst:** Object of class "MosaicsFitEst", representing estimates of MOSAiCS model fit.
- init:** Object of class "character", representing the approach to initialize MOSAiCS-HMM.
- initPiMat:** Object of class "numeric", representing initial transition matrix.
- peakParam:** Object of class "MosaicsPeakParam", representing parameters for peak calling.
- binsize:** Object of class "numeric", representing size of a bin.
- nRatio:** Object of class "numeric", representing ratio of sequencing depth of ChIP vs. control.

bicMosaics: Object of class "numeric", representing the BIC value of MOSAiCS fit.
bicMosaicsHMM: Object of class "numeric", representing the BIC value of MOSAiCS-HMM fit.
seqDepth: Object of class "numeric", a vector of sequencing depth of length 2, where the first and second elements correpond to sequencing depths of ChIP and control samples, respectively. If there is not control sample, the second element is set to NA.

Methods

estimates signature(object = "MosaicsHMM"): extract estimates from MOSAiCS-HMM model fit. =
plot signature(x = "MosaicsHMM", y = "missing", seed=12345, parallel=FALSE, nCore=8): draw Goodness of Fit (GOF) plot. You can specify random seed in seed. If parallel=TRUE, parallel computing is utilized to simulate data, where nCore indicates CPUs used for parallel computing.
print signature(x = "MosaicsHMM"): (not supported yet)
show signature(object = "MosaicsHMM"): provide brief summary of the object.
seqDepth signature(object = "MosaicsHMM"): provide a vector of sequencing depth.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.
Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFitHMM](#), [mosaicsPeakHMM](#).

Examples

```
showClass("MosaicsHMM")
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=".",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc=".",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
```

```

PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip","input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binHM
plot(binHM)
plot( binHM, plotType="input" )

fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
fitHM
plot(fitHM)

hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
hmmHM
plot(hmmHM)

peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata","wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), pa
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata","wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam")
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
head(print(peakHM))
plot( peakHM, filename="./peakplot_HM.pdf" )

peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

export( peakHM, type = "txt", filename = "./peakHM.txt" )
export( peakHM, type = "bed", filename = "./peakHM.bed" )
export( peakHM, type = "gff", filename = "./peakHM.gff" )
export( peakHM, type = "narrowPeak", filename = "./peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = "./peakHM.broadPeak" )

## End(Not run)

```

Description

Call peaks using `MosaicsFit` class object, which is a fitted MOSAiCS model.

Usage

```
mosaicsPeak( object, ... )
## S4 method for signature 'MosaicsFit'
mosaicsPeak( object, signalModel="2S", FDR=0.05,
             binsize=NA, maxgap=200, minsize=50, thres=10 )
```

Arguments

| | |
|--------------------------|---|
| <code>object</code> | Object of class <code>MosaicsFit</code> , a fitted MOSAiCS model obtained using function <code>mosaicsFit</code> . |
| <code>signalModel</code> | Signal model. Possible values are "1S" (one-signal-component model) and "2S" (two-signal-component model). Default is "2S". |
| <code>FDR</code> | False discovery rate. Default is 0.05. |
| <code>binsize</code> | Size of each bin. Value should be positive integer. If <code>binsize=NA</code> , <code>mosaicsPeak</code> function calculates the value from data. Default is NA. |
| <code>maxgap</code> | Initial nearby peaks are merged if the distance (in bp) between them is less than <code>maxgap</code> . Default is 200. |
| <code>minsize</code> | An initial peak is removed if its width is narrower than <code>minsize</code> . Default is 50. |
| <code>thres</code> | A bin within initial peak is removed if its ChIP tag counts are less than <code>thres</code> . Default is 10. |
| <code>...</code> | Other parameters to be passed through to generic <code>mosaicsPeak</code> . |

Details

`mosaicsPeak` is developed to identify narrow peaks such as transcription factor binding sites. If you are interested in identifying broad peaks such as histone modifications, please use `mosaicsFitHMM` and `mosaicsPeakHMM` instead of `mosaicsPeak`.

When peaks are called, proper signal model needs to be specified. The optimal choice for the number of signal components depends on the characteristics of ChIP-seq data. In order to support users in the choice of optimal signal model, Bayesian Information Criterion (BIC) values and Goodness of Fit (GOF) plot are provided for the fitted MOSAiCS model. BIC values and GOF plot can be obtained by applying `show` and `plot` methods, respectively, to the `MosaicsFit` class object, which is a fitted MOSAiCS model.

`maxgap`, `minsize`, and `thres` are for refining initial peaks called using specified `signalModel` and `FDR`. If you use a bin size shorter than the average fragment length of the experiment, we recommend to set `maxgap` to the average fragment length and `minsize` to the bin size. If you set the bin size to the average fragment length or if bin size is larger than the average fragment length, set `maxgap` to the average fragment length and `minsize` to a value smaller than the average fragment length. See the vignette for further details.

Value

Construct `MosaicsPeak` class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFit](#), [MosaicsPeak](#), [MosaicsFit](#).

Examples

```
## Not run:
library(mosaicsExample)
data(exampleBinData)
exampleFit <- mosaicsFit( exampleBinData, analysisType="IO" )
examplePeak <- mosaicsPeak( exampleFit, signalModel = "2S", FDR = 0.05 )

## End(Not run)
```

MosaicsPeak-class *Class "MosaicsPeak"*

Description

This class represents peak calling results.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsPeak", ...)`.

Slots

peakList: Object of class `"data.frame"`, representing peak list.
chrID: Object of class `"character"`, a vector of chromosome IDs.
coord: Object of class `"numeric"`, a vector of genomic coordinates.
tagCount: Object of class `"numeric"`, a vector of tag counts of ChIP sample.
mappability: Object of class `"numeric"`, a vector of mappability score.
gcContent: Object of class `"numeric"`, a vector of GC content score.
input: Object of class `"numeric"`, a vector of tag counts of matched control sample.

peakParam: Object of class "MosaicsPeakParam", representing parameters for peak calling.

bdBin: Object of class "numeric", representing a vector of bounded bins.

empFDR: Object of class "numeric", representing empirical FDR.

postProb: Object of class "numeric", representing posterior probability that a bin belongs to background.

tagLoaded: Object of class "logical", representing whether read-level data is loaded.

tagData: Object of class "TagData", representing read-level data.

seqDepth: Object of class "numeric", a vector of sequencing depth of length 2, where the first and second elements correpond to sequencing depths of ChIP and control samples, respectively. If there is not control sample, the second element is set to NA.

Methods

export signature(object = "MosaicsPeak"): export peak list into text files.

print signature(x = "MosaicsPeak"): return peak list in data frame format.

plot signature(x = "MosaicsPeak", y = "missing", filename=NA, peakNum=NA): plot ChIP profile in each peak region. If file name is specified in filename, plots are exported to a PDF file named filename. Oterwise, ChIP profiles are plotted to standard output. If users are interested in specific peak regions, users can specify them as a vector in peakNum, where elements indicate which rows peak regions of interest are located. If peakNum is specified, only ChIP profiles in specified peak regions are plotted. Otherwise, ChIP profiles for all the peak regions are plotted.

show signature(object = "MosaicsPeak"): provide brief summary of the object.

empFDR signature(object = "MosaicsPeak"): return estimated empirical false discovery rate.

bdBin signature(object = "MosaicsPeak"): return a vector of bin-level binary indicator of peak calling, where each element is 1 if the corresponding bin belongs to a peak and zero otherwise.

readCoverage signature(object = "MosaicsPeak"): export a list of coverage matrices of ChIP and matched control samples, where each matrix consists of two columns, genomic coordinates and read count. Each element of this list is a list of length 2, which are matrices for each of ChIP and matched control samples. Elements of this list are sorted to match the rows of peak list. Users can use readCoverage method only after extractReads method is applied to the MosaicsPeak object.

read signature(object = "MosaicsPeak"): return a list of read-level data of ChIP and matched control samples, where each element is GenomicRanges class. Each element of this list is a list of length 2, which are GenomicRanges objects for each of ChIP and matched control samples. Elements of this list are sorted to match the rows of peak list. Users can use read method only after extractReads method is applied to the MosaicsPeak object.

seqDepth signature(object = "MosaicsPeak"): return a vector of sequencing depth, where the first and second elements are for ChIP and matched control sample, respectively. If matched control sample is not provided, the second element is NA. Users can use seqDepth method only after extractReads method is applied to the MosaicsPeak object.

postProb signature(object = "MosaicsPeak" , peakRegion=NULL , summaryStat="aveLogP" , parallel=FALSE , nCore=8): return a data frame of peak-level posterior probabilities of being background (PP) for arbitrary peak regions, where the columns are chromosome ID, peak start position, and peak end position, and summary of PP. Peak regions of interest can be specified in peakRegion argument and a data frame of three columns (chromosome ID, peak start position, and peak end position) is expected. If peakRegion is not provided, a data frame of bin-level PP is provided, where columns are chromosome ID, genomic coordinate, and PP. Summary statistics can be chosen among "aveLogP" (average of -log10 transformed PP; default), "medianLogP" (median of -log10 transformed PP), "sumLogP" (sum of -log10 transformed PP), "logMinP" (-log10 transformation of minimum PP), "logAveP" (-log10 transformation of average PP), and "logMedianP" (-log10 transformation of median PP). Multiple CPUs can be used for parallel computing using "parallel" package if parallel=TRUE, where the number of cores to be used can be specified using nCore.

seqDepth signature(object = "MosaicsPeak"): provide a vector of sequencing depth.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [export](#), [extractReads](#), [findSummit](#), [adjustBoundary](#), [filterPeak](#).

Examples

```
showClass("MosaicsPeak")
## Not run:
library(mosaicsExample)

# example analysis workflow for ChIP-seq data of transcription factor binding
# (STAT1 factor binding in GM12878 cell line, from ENCODE database)

generateWig( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAlnRep1_chr22_sorted.bam"))
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, span=200, capping=0, normConst=1 )

constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAlnRep1_chr22_sorted.bam")
  fileFormat="bam", outfileLoc="./",
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878InputStdAlnRep1_chr22_sorted.bam")
  fileFormat="bam", outfileLoc="./",
```

```

PET=FALSE, fragLen=200, binSize=200, capping=0 )

binTFBS <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binTFBS
head(print(binTFBS))
plot(binTFBS)
plot( binTFBS, plotType="input" )

fitTFBS <- mosaicsFit( binTFBS, analysisType="IO", bgEst="rMOM" )
fitTFBS
plot(fitTFBS)

peakTFBS <- mosaicsPeak( fitTFBS, signalModel="2S", FDR=0.05,
maxgap=200, minsize=50, thres=10 )
peakTFBS
head(print(peakTFBS))

peakTFBS <- extractReads( peakTFBS,
  chipFile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam"), package=""),
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam"), package=""),
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakTFBS

peakTFBS <- findSummit( peakTFBS, parallel=FALSE, nCore=8 )

export( peakTFBS, type = "txt", filename = "./peakTFBS.txt" )
export( peakTFBS, type = "bed", filename = "./peakTFBS.bed" )
export( peakTFBS, type = "gff", filename = "./peakTFBS.gff" )
export( peakTFBS, type = "narrowPeak", filename = "./peakTFBS.narrowPeak" )

# example analysis workflow for ChIP-seq data of histone modification
# (H3K4me3 modification in GM12878 cell line, from ENCODE database)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binHM
plot(binHM)
plot( binHM, plotType="input" )

fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )

```

```

fitHM
plot(fitHM)

hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
hmmHM
plot(hmmHM)

peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAInRep1_chr22_sorted.bam"), package="ENSG", mustWork=TRUE ),
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAInRep1_chr22_sorted.bam"), package="ENSG", mustWork=TRUE ),
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
head(print(peakHM))
plot( peakHM, filename="./peakplot_HM.pdf" )

peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

export( peakHM, type = "txt", filename = "./peakHM.txt" )
export( peakHM, type = "bed", filename = "./peakHM.bed" )
export( peakHM, type = "gff", filename = "./peakHM.gff" )
export( peakHM, type = "narrowPeak", filename = "./peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = "./peakHM.broadPeak" )

## End(Not run)

```

mosaicsPeakHMM

Call broad peaks using fitted MOSAiCS-HMM model

Description

Call broad peaks using `MosaicsHMM` class object, which is a fitted MOSAiCS-HMM model.

Usage

```

mosaicsPeakHMM( object, ... )
## S4 method for signature 'MosaicsHMM'
mosaicsPeakHMM( object, FDR=0.05, decoding="posterior",

```

```
  binsize=NA, maxgap=0, minsize=0, thres=0,
  parallel=FALSE, nCore=8 )
```

Arguments

| | |
|----------|---|
| object | Object of class MosaicsHMM, a fitted MOSAiCS model obtained using function mosaicsFitHMM. |
| FDR | False discovery rate. Default is 0.05. Not relevant when decoding="viterbi". |
| decoding | Approach to determine the undelying state. Possible values are "viterbi" (Viterbi algorithm) and "posterior" (posterior decoding). Default is "posterior". |
| binsize | Size of each bin. Value should be positive integer. If binsize=NA, mosaicsPeakHMM function calcuates the value from data. Default is NA. |
| maxgap | Initial nearby peaks are merged if the distance (in bp) between them is less than maxgap. Default is 0. |
| minsize | An initial peak is removed if its width is narrower than minsize. Default is 0. |
| thres | A bin within initial peak is removed if its ChIP tag counts are less than thres. Default is 0. |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (utilize multiple CPUs) or FALSE (do not utilize multiple CPUs). Default is FALSE (do not utilize multiple CPUs). |
| nCore | Number of CPUs when parallel computing is utilized. |
| ... | Other parameters to be passed through to generic mosaicsHMM. |

Details

mosaicsFitHMM and mosaicsPeakHMM are developed to identify broad peaks such as histone modifications, using Hidden Markov Model (HMM) approach, as proposed in Chung et al. (2014). If you are interested in identifying narrow peaks such as transcription factor binding sites, please use mosaicsPeak instead of mosaicsFitHMM and mosaicsPeakHMM.

maxgap, minsize, and thres are for refining initial peaks called using specified decoding (and FDR if decoding="posterior"). If you use a bin size shorter than the average fragment length of the experiment, we recommend to set maxgap to the average fragment length and minsize to the bin size. If you set the bin size to the average fragment length or if bin size is larger than the average fragment length, set maxgap to the average fragment length and minsize to a value smaller than the average fragment length. See the vignette for further details.

Parallel computing can be utilized for faster computing if parallel=TRUE and parallel package is loaded. nCore determines number of CPUs used for parallel computing.

Value

Construct MosaicsPeak class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsFitHMM](#), [extractReads](#), [findSummit](#), [adjustBoundary](#), [filterPeak](#), [MosaicsHMM](#), [MosaicsPeak](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAlnRep1_chr22_sorted"),
  fileFormat="bam", outfileLoc="./",
  byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  PET=FALSE, fragLen=200, binSize=200, capping=0 )

binHM <- readBins( type=c("chip", "input"),
  fileName=c( "./wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted.bam_fragL200_bin200.txt",
  "./wgEncodeBroadHistoneGm12878ControlStdAlnRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )
binHM
plot(binHM)
plot( binHM, plotType="input" )

fitHM <- mosaicsFit( binHM, analysisType="IO", bgEst="rMOM" )
fitHM
plot(fitHM)

hmmHM <- mosaicsFitHMM( fitHM, signalModel = "2S",
  init="mosaics", init.FDR = 0.05, parallel=TRUE, nCore=8 )
hmmHM
plot(hmmHM)

peakHM <- mosaicsPeakHMM( hmmHM, FDR = 0.05, decoding="posterior",
  thres=10, parallel=TRUE, nCore=8 )

peakHM <- extractReads( peakHM,
  chipFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878H3k4me3StdAlnRep1_chr22_sorted.bam"), package="mosaics"),
  chipFileFormat="bam", chipPET=FALSE, chipFragLen=200,
  controlFile=system.file( file.path("extdata", "wgEncodeBroadHistoneGm12878ControlStdAlnRep1_chr22_sorted.bam"), package="mosaics"),
  controlFileFormat="bam", controlPET=FALSE, controlFragLen=200, parallel=TRUE, nCore=8 )
peakHM
```

```

peakHM <- findSummit( peakHM, parallel=TRUE, nCore=8 )
head(print(peakHM))
plot( peakHM, filename=".~/peakplot_HM.pdf" )

peakHM <- adjustBoundary( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

peakHM <- filterPeak( peakHM, parallel=TRUE, nCore=8 )
peakHM
head(print(peakHM))

export( peakHM, type = "txt", filename = ".~/peakHM.txt" )
export( peakHM, type = "bed", filename = ".~/peakHM.bed" )
export( peakHM, type = "gff", filename = ".~/peakHM.gff" )
export( peakHM, type = "narrowPeak", filename = ".~/peakHM.narrowPeak" )
export( peakHM, type = "broadPeak", filename = ".~/peakHM.broadPeak" )

## End(Not run)

```

MosaicsPeakParam-class

Class "*MosaicsPeakParam*"

Description

This class represents parameters for mosaicsPeak function.

Objects from the Class

Objects can be created by calls of the form `new("MosaicsPeakParam", ...)`.

Slots

analysisType: Object of class "character", representing type of data analysis.
signalModel: Object of class "character", representing signal model for peak calling.
FDR: Object of class "numeric", representing specified false discovery rate.
maxgap: Object of class "numeric", representing maximum gap size to combine two neighboring initial peaks.
minsize: Object of class "numeric", representing minimum peak size to be remained in the final peak list.
thres: Object of class "numeric", representing threshold of ChIP tag count to filter initial peaks.
decoding: Object of class "character", representing decoding approach for MOSAiCS-HMM peak calling.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [MosaicsPeak](#).

Examples

```
showClass("MosaicsPeakParam")
```

| | |
|-------------------------------|---|
| mosaicsRunAll | Analyze ChIP-seq data using the MOSAiCS framework |
|-------------------------------|---|

Description

Construct bin-level ChIP-seq data from aligned read files of ChIP and matched control samples, fit a MOSAiCS model, call peaks, export peak calling results, and generate reports for diagnostics.

Usage

```
mosaicsRunAll(
  chipFile=NULL, chipFileFormat=NULL,
  controlFile=NULL, controlFileFormat=NULL,
  binfileDir=NULL,
  peakFile=NULL, peakFileFormat=NULL,
  reportSummary=FALSE, summaryFile=NULL,
  reportExploratory=FALSE, exploratoryFile=NULL,
  reportGOF=FALSE, gofFile=NULL,
  PET=FALSE, byChr=FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr=NULL,
  FDR=0.05, fragLen=200, binSize=200, capping=0, bgEst="rMOM", d=0.25,
  signalModel="BIC", maxgap=200, minsize=50,
  thres=10, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|-------------------|---|
| chipFile | Name of the aligned read file of ChIP sample to be processed. |
| chipFileFormat | Format of the aligned read file of ChIP sample to be processed. Currently, mosaicsRunAll permits the following aligned read file formats: "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bed" (BED), and "csem" (CSEM BED). Note that "csem" does not mean CSEM output file format, but CSEM BED file format. |
| controlFile | Name of the aligned read file of matched control sample to be processed. |
| controlFileFormat | Format of the aligned read file of matched control sample to be processed. Currently, mosaicsRunAll permits the following aligned read file formats: "eland_result" (Eland result), "eland_extended" (Eland extended), "eland_export" (Eland export), "bowtie" (default Bowtie), "sam" (SAM), "bed" (BED), and "csem" (CSEM BED). Note that "csem" does not mean CSEM output file format, but CSEM BED file format. |
| binfileDir | Directory to store processed bin-level files. |
| peakFile | Name of the peak list generated from the analysis. |
| peakFileFormat | Format of the peak list generated from the analysis. Possible values are "txt", "bed", and "gff". |
| reportSummary | Report the summary of model fitting and peak calling? Possible values are TRUE (YES) and FALSE (NO). Default is FALSE (NO). |
| summaryFile | File name of the summary report of model fitting and peak calling. The summary report is a text file. |
| reportExploratory | Report the exploratory analysis plots? Possible values are TRUE (YES) and FALSE (NO). Default is FALSE (NO). |
| exploratoryFile | Name of the file for exploratory analysis plots. The exploratory analysis results are exported as a PDF file. |
| reportGOF | Report the goodness of fit (GOF) plots? Possible values are TRUE (YES) and FALSE (NO). Default is FALSE (NO). |
| gofFile | Name of the file for goodness of fit (GOF) plots. The GOF plots are exported as a PDF file. |
| PET | Is the file paired-end tag (PET) data? If PET=FALSE, it is assumed that the file is SET data. If PET=TRUE, it is assumed that the file is PET data. Default is FALSE (SET data). |
| byChr | Analyze ChIP-seq data for each chromosome separately or analyze it genome-wide? Possible values are TRUE (chromosome-wise) and FALSE (genome-wide). Default is FALSE (genome-wide analysis). |
| useChrfile | Is the file for chromosome info provided? Possible values are TRUE or FALSE. If useChrfile=FALSE, it is assumed that the file for chromosome info is not provided. If useChrfile=TRUE, it is assumed that the file for chromosome info is provided. Default is FALSE. |

| | |
|-------------|---|
| chrfile | Name of the file for chromosome info. In this file, the first and second columns are ID and size of each chromosome, respectively. |
| excludeChr | Vector of chromosomes that will be excluded from the analysis. |
| FDR | False discovery rate. Default is 0.05. |
| fragLen | Average fragment length. Default is 200. |
| binSize | Size of bins. Default is 200. |
| capping | Maximum number of reads allowed to start at each nucleotide position. To avoid potential PCR amplification artifacts, the maximum number of reads that can start at a nucleotide position is capped at capping. Capping is not applied if non-positive capping is used. Default is 0 (no capping). |
| bgEst | Parameter to determine background estimation approach. Possible values are "matchLow" (estimation using bins with low tag counts) and "rMOM" (estimation using robust method of moment (MOM)). If bgEst="automatic", this method tries to make the best guess for bgEst, based on the data provided. Default is bgEst="rMOM". |
| d | Parameter for estimating background distribution. Default is 0.25. |
| signalModel | Signal model. Possible values are "BIC" (automatic model selection using BIC), "1S" (one-signal-component model), and "2S" (two-signal-component model). Default is "BIC". |
| maxgap | Initial nearby peaks are merged if the distance (in bp) between them is less than maxgap. Default is 200. |
| minsize | An initial peak is removed if its width is narrower than minsize. Default is 50. |
| thres | A bin within initial peak is removed if its ChIP tag counts are less than thres. Default is 10. |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (use multiple CPUs) or FALSE (do not use multiple CPUs). Default is FALSE (do not use multiple CPUs). |
| nCore | Number of maximum number of CPUs used for the analysis. Default is 8. |

Details

This method implements the work flow for the two-sample analysis of ChIP-seq data using the MO-SAiCS framework (without using mappability and GC content scores). It imports aligned read files of ChIP and matched control samples, processes them into bin-level files, fits MOSAiCS model, calls peaks, exports the peak lists to text files, and generates reports for diagnostics. This method is a wrapper function of `constructBins`, `readBins`, `mosaicsFit`, `mosaicsPeak`, `export` functions, and methods of `BinData`, `MosaicsFit`, and `MosaicsPeak` classes.

See the vignette of the package for the illustration of the work flow and the description of employed methods and their options. Exploratory analysis plots and goodness of fit (GOF) plots are generated using the methods `plot` of the classes `BinData` and `MosaicsFit`, respectively. See the help of `constructBins` for details of the options `PET`, `chipFileFormat`, `controlFileFormat`, `byChr`, `useChrfile`, `chrfile`, `excludeChr`, `fragLen`, `binSize`, and `capping`. See the help of `mosaicsFit` for details of the options `bgEst` and `d`. See the help of `mosaicsPeak` for details of the options `FDR`, `signalModel`, `maxgap`, `minsize`, and `thres`. See the help of `export` for details of the option `peakFileFormat`.

When the data contains multiple chromosomes, parallel computing can be utilized for faster pre-processing and model fitting if `parallel=TRUE` and `parallel` package is loaded. `nCore` determines number of CPUs used for parallel computing.

Value

Processed bin-level files are exported to the directory specified in `binfileDir` argument. If `byChr=FALSE` (genome-wide analysis), one bin-level file is generated for each of ChIP and matched control samples, where file names are `[chipFile]_fragL[fragLen]_bin[binSize].txt` and `[controlFile]_fragL[fragLen]_bin[binSize].txt`, respectively, for SET data (`PET = FALSE`). For PET data (`PET = TRUE`), file names for each of ChIP and matched control samples are `[chipFile]_bin[binSize].txt` and `[controlFile]_bin[binSize].txt`, respectively. If `byChr=TRUE` (chromosome-wise analysis), bin-level files are generated for each chromosome of each of ChIP and matched control samples, where file names are `[chipFile]_fragL[fragLen]_bin[binSize]_[chrID].txt` and `[controlFile]_fragL[fragLen]_bin[binSize]_[chrID].txt`, respectively, for SET data (`PET = FALSE`) (`[chrID]` is chromosome IDs that reads align to). For PET data (`PET = TRUE`), file names for each of ChIP and matched control samples are `[chipFile]_bin[binSize]_[chrID].txt` and `[controlFile]_bin[binSize]_[chrID].txt`, respectively.

The peak list generated from the analysis are exported to the file with the name specified in `peakFile`. If `reportSummary=TRUE`, the summary of model fitting and peak calling is exported to the file with the name specified in `summaryFile` (text file). If `reportExploratory=TRUE`, the exploratory analysis plots are exported to the file with the name specified in `exploratoryFile` (PDF file). If `reportGOF=TRUE`, the goodness of fit (GOF) plots are exported to the file with the name specified in `gofFile` (PDF file).

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[constructBins](#), [readBins](#), [mosaicsFit](#), [mosaicsPeak](#), [export](#), [BinData](#), [MosaicsFit](#), [MosaicsPeak](#).

Examples

```
## Not run:
# minimal input (without any reports for diagnostics)

mosaicsRunAll(
  chipFile = "/scratch/eland/STAT1_eland_results.txt",
  chipFileFormat = "eland_result",
```

```

controlFile = "/scratch/eland/input_eland_results.txt",
controlFileFormat = "eland_result",
binfileDir = "/scratch/bin/",
peakFile = "/scratch/peak/STAT1_peak_list.bed",
peakFileFormat = "bed" )

# generate all reports for diagnostics

library(parallel)
mosaicsRunAll(
  chipFile = "/scratch/eland/STAT1_eland_results.txt",
  chipFileFormat = "eland_result",
  controlFile = "/scratch/eland/input_eland_results.txt",
  controlFileFormat = "eland_result",
  binfileDir = "/scratch/bin/",
  peakFile = "/scratch/peak/STAT1_peak_list.bed",
  peakFileFormat = "bed",
  reportSummary = TRUE,
  summaryFile = "/scratch/reports/mosaics_summary.txt",
  reportExploratory = TRUE,
  exploratoryFile = "/scratch/reports/mosaics_exploratory.pdf",
  reportGOF = TRUE,
  gofFile = "/scratch/reports/mosaics_GOF.pdf",
  PET = FALSE, byChr = FALSE, useChrfile=FALSE, chrfile=NULL, excludeChr = "chrM",
  FDR = 0.05, fragLen = 200, capping = 0, bgEst="automatic", thres=10,
  parallel = TRUE, nCore = 8 )

## End(Not run)

```

readBins*Import bin-level ChIP-sep data*

Description

Import and preprocess all or subset of bin-level ChIP-sep data, including ChIP data, matched control data, mappability score, GC content score, and sequence ambiguity score.

Usage

```
readBins( type = c("chip", "input"), fileName = NULL,
  dataType = "unique", rounding = 100, parallel=FALSE, nCore=8 )
```

Arguments

| | |
|------|--|
| type | Character vector indicating data types to be imported. This vector can contain "chip" (ChIP data), "input" (matched control data), "M" (mappability score), "GC" (GC content score), and "N" (sequence ambiguity score). Currently, readBins permits only the following combinations: c("chip", "input"), c("chip", "input", "N"), c("chip", "input", "M", "GC", "N"), and c("chip", "M", "GC", "N"). Default is c("chip", "input"). |
|------|--|

| | |
|----------|---|
| fileName | Character vector of file names, each of which matches each element of type. type and fileName should have the same length and corresponding elements in two vectors should appear in the same order. |
| dataType | How reads were processed? Possible values are either "unique" (only uniquely aligned reads were retained) or "multi" (reads aligned to multiple locations were also retained). |
| rounding | How are mappability score and GC content score rounded? Default is 100 and this indicates rounding of mappability score and GC content score to the nearest hundredth. |
| parallel | Utilize multiple CPUs for parallel computing using "parallel" package? Possible values are TRUE (use multiple CPUs) or FALSE (do not use multiple CPUs). Default is FALSE (do not use multiple CPUs). |
| nCore | Number of CPUs when parallel computing is utilized. |

Details

Bin-level ChIP and matched control data can be generated from the aligned read files for your samples using the method `constructBins`. In `mosaics` package companion website, <http://www.stat.wisc.edu/~keles/Software/mosaics/>, we provide preprocessed mappability score, GC content score, and sequence ambiguity score files for diverse reference genomes. Please check the website and the vignette for further details.

The imported data type constraints the analysis that can be implemented. If `type=c("chip", "input")` or `c("chip", "input", "N")`, only two-sample analysis without using mappability and GC content is allowed. For `type=c("chip", "input", "M", "GC", "N")`, user can do the one- or two-sample analysis. If `type=c("chip", "M", "GC", "N")`, only one-sample analysis is permitted. See help page of `mosaicsFit`.

When the data contains multiple chromosomes, parallel computing can be utilized for faster pre-processing if `parallel=TRUE` and `parallel` package is loaded. `nCore` determines number of CPUs used for parallel computing.

Value

Construct `BinData` class object.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[constructBins](#), [mosaicsFit](#), [BinData](#).

Examples

```
## Not run:
library(mosaicsExample)

constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam",
                                             fileFormat="bam", outfileLoc="./",
                                             PET=FALSE, fragLen=200, binSize=200, capping=0 )
constructBins( infile=system.file( file.path("extdata", "wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam",
                                             fileFormat="bam", outfileLoc="./",
                                             PET=FALSE, fragLen=200, binSize=200, capping=0 )

binTFBS <- readBins( type=c("chip", "input"),
                      fileName=c( "wgEncodeSydhTfbsGm12878Stat1StdAInRep1_chr22_sorted.bam_fragL200_bin200.txt",
                                 "wgEncodeSydhTfbsGm12878InputStdAInRep1_chr22_sorted.bam_fragL200_bin200.txt" ) )

## End(Not run)
```

TagData-class

Class "TagData"

Description

This class represents read-level ChIP-seq data.

Objects from the Class

Objects can be created by calls of the form `new("TagData", ...)`.

Slots

coverage: Object of class "list", a list of read coverage, where each element is a list including ChIP and matched control samples.

numReads: Object of class "numeric", a matrix of number of reads in peak regions, where rows correspond to peak regions and columns correspond to ChIP and matched control samples.

read: Object of class "list", a list of read-level data, where each element is a list including ChIP and matched control samples.

keepReads: Object of class "logical", representing whether to keep read-level data.

Author(s)

Dongjun Chung, Pei Fen Kuan, Rene Welch, Sunduz Keles

References

Kuan, PF, D Chung, G Pan, JA Thomson, R Stewart, and S Keles (2011), "A Statistical Framework for the Analysis of ChIP-Seq Data", *Journal of the American Statistical Association*, Vol. 106, pp. 891-903.

Chung, D, Zhang Q, and Keles S (2014), "MOSAiCS-HMM: A model-based approach for detecting regions of histone modifications from ChIP-seq data", Datta S and Nettleton D (eds.), *Statistical Analysis of Next Generation Sequencing Data*, Springer.

See Also

[mosaicsPeak](#), [mosaicsPeakHMM](#), [extractReads](#), [findSummit](#), [filterPeak](#), [MosaicsPeak](#).

Examples

```
showClass("TagData")
```

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