Package 'segmenter'

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Type Package

Title Perform Chromatin Segmentation Analysis in R by Calling ChromHMM

Version 1.17.0

Description Chromatin segmentation analysis transforms ChIP-seq data into signals over the genome. The latter represents the observed states in a multivariate Markov model to predict the chromatin's underlying states. ChromHMM, written in Java, integrates histone modification datasets to learn the chromatin states de-novo. The goal of this package is to call chromHMM from within R, capture the output files in an S4 object and interface to other relevant Bioconductor analysis tools. In addition, segmenter provides functions to test, select and visualize the output of the segmentation.

License GPL-3 Encoding UTF-8 RoxygenNote 7.1.1 Depends R (>= 4.1)

BugReports https://github.com/MahShaaban/segmenter/issues

Suggests testthat, knitr, rmarkdown,

TxDb.Hsapiens.UCSC.hg18.knownGene, Gviz

Imports ChIPseeker, GenomicRanges, SummarizedExperiment, IRanges, S4Vectors, bamsignals, ComplexHeatmap, graphics, stats, utils, methods, chromhmmData

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biocViews Software, HistoneModification

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.Binarize 3

Description

Call the Java module BinarizeBed which binarize a bed file of the aligned reads.

Usage

```
.Binarize(inputdir, cellmarkfiletable, chromsizefile, binsize, outputdir, type)
```

Arguments

inputdir A string. The path to bed files.

cellmarkfiletable

A tab delimited files of three columns. The columns contains the cell, mark and

the name or the bed file.

 $\label{lem:chromosomes} \mbox{chromosomes sizes file.}$

binsize An integer. The bin size to use. Default is 200.

outputdir A string. The path to a directory where output will be written.

type A string. The file type 'bam' or 'bed'.

Value

NULL. Output files are written to the output directory.

See Also

binarize_bed

.LearnModel	Call Java LearnModel	

Description

Call the Java module LearnModel which learns a multi-state model from ChIP-seq data.

4 accessors

Usage

```
.LearnModel(
  inputdir,
  outputdir,
  numstates,
  coordsdir,
  anchorsdir,
  chromsizefile,
  assembly,
  optional
)
```

Arguments

inputdir A string. The path to binarized files.

outputdir A string. The path to a directory where output will be written.

numstates An integer. The number of desired states in the model.

coordsdir A string. The path to genomic coordinates files.

anchorsdir A string. The path to the genomic anchors files.

chromsizefile A string. The path to the chromosomes sizes file.

A string. The name of the genomic assembly.

optional A string. Other optional arguments passed to the Java command.

Value

NULL. Output files are written to the output directory.

See Also

learn_model

accessors

Accessors for the segmentation objects

Description

These functions can be used to access the contents of segmentation objects as well as modifying them.

accessors 5

Usage

```
model(object)
## S4 method for signature 'segmentation'
model(object)
emission(object)
## S4 method for signature 'segmentation'
emission(object)
transition(object)
## S4 method for signature 'segmentation'
transition(object)
overlap(object, ...)
## S4 method for signature 'segmentation'
overlap(object, cell)
TSS(object, ...)
## S4 method for signature 'segmentation'
TSS(object, cell)
TES(object, ...)
## S4 method for signature 'segmentation'
TES(object, cell)
segment(object, ...)
## S4 method for signature 'segmentation'
segment(object, cell)
bins(object, ...)
## S4 method for signature 'segmentation'
bins(object, cell)
counts(object, ...)
## S4 method for signature 'segmentation'
counts(object, cell)
likelihood(object)
```

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```
## S4 method for signature 'segmentation'
likelihood(object)

cells(object)

## S4 method for signature 'segmentation'
cells(object)

states(object)

## S4 method for signature 'segmentation'
states(object)

markers(object)

## S4 method for signature 'segmentation'
markers(object)
```

Arguments

object An object of class segmentation
... Other argument passed to the accessors
cell A string

Value

The data in the corresponding slot or a subset of it.

See Also

segmentation

```
model(test_obj)
emission(test_obj)
transition(test_obj)
overlap(test_obj)
overlap(test_obj, cell = 'K562')
TSS(test_obj)
TSS(test_obj, cell = 'K562')
TES(test_obj, cell = 'K562')
Segment(test_obj)
```

annotate_segments 7

```
segment(test_obj, cell = 'K562')
bins(test_obj)
counts(test_obj)
likelihood(test_obj)
cells(test_obj)
states(test_obj)
markers(test_obj)
```

annotate_segments

Annotate segments

Description

Annotate the GRanges objects of the segments using annotatePeak (see for details)

Usage

```
annotate_segments(segments, ...)
```

Arguments

segments A GRanges object. Usually the output of calling segment on the the output object of lean_model.

... Other arguments passed to annotatePeak

Value

A GRanges object which is identical to the input in addition to the annotations as metadata columns.

```
library(TxDb.Hsapiens.UCSC.hg18.knownGene)
txdb <- TxDb.Hsapiens.UCSC.hg18.knownGene
segs <- segment(test_obj)
segs_annotated <- annotate_segments(segs, TxDb = txdb, verbose = FALSE)</pre>
```

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binarize_bam

Binarize the bam files

Description

Transform the aligned reads into a binary format.

Usage

```
binarize_bam(
  inputdir,
  cellmarkfiletable,
  chromsizefile,
  binsize = 200,
  outputdir
)
```

Arguments

Value

NULL. Write files to the outputdir

See Also

Binarize binarize_bed

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binarize_bed

Binarize the bed files

Description

Transform the aligned reads into a binary format.

Usage

```
binarize_bed(
  inputdir,
  cellmarkfiletable,
  chromsizefile,
  binsize = 200,
  outputdir
)
```

Arguments

inputdir A string. The directory of the bam files.

cell mark file table

A string. The path to the input files table. Only

chromsizefile A string. The path to the chromosomes sizes file.

binsize An integer. The number in bp used to generate binarized files.

outputdir A string. The path to a directory where output will be written.

Value

NULL. Write files to the outputdir

See Also

Binarize binarize_bam

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compare_models

Compare two or more models

Description

Compare two or more models

Usage

```
compare_models(objs, type = "emission", plot = FALSE, ...)
```

Arguments

objs A list of segmentation items

type A string. What to compare. Default to 'emission'

plot A logical.

... Other arguments passed to plot

Value

A numeric vector or a plot with the same values.

Examples

```
compare_models(test_objs)
compare_models(test_objs, type = 'likelihood')
```

count_reads_ranges

Count reads in GRanges objects from bam files

Description

Count reads in GRanges objects from bam files

Usage

```
count_reads_ranges(ranges, cellmarkfiletable, inputbamdir)
```

Arguments

ranges A GRanges to count in.

cellmarkfiletable

A string. The path to the input files table.

inputbamdir A string. The path to the input bam files directory.

emissions_file 11

Value

A SummarizedExperiment object with ranges as its rowRanges and the counts as the assay.

 ${\tt emissions_file}$

Make emissions file name

Description

Make emissions file name

Usage

```
emissions_file(numstates)
```

Arguments

numstates

An integer

Value

A string

Examples

```
emissions_file(3)
```

 $enrichment_files$

Make enrichment file names

Description

Make enrichment file names

Usage

```
enrichment_files(numstates, cells, table = "RefSeq", annotation = "TSS")
```

Arguments

numstates An integer

cells A character vector

table A string annotation A string

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Value

A character vector

Examples

```
enrichment_files(3, 'K562')
```

get_frequency

Get the frequency of the segments in each cell type

Description

Get the frequency of the segments in each cell type

Usage

```
get_frequency(segments, normalize = FALSE, tidy = FALSE, plot = FALSE, ...)
```

Arguments

segments A GRanges object. Usually the output of calling segment on the the output

object of lean_model.

normalize A logical. Whether the frequency should be normalized by the total number of

segments

tidy A logical.
plot A logical.

... Other arguments passed to barplot

Value

A data. frame when tidy is TRUE otherwise a matrix or a plot

```
get_frequency(segment(test_obj))
get_frequency(segment(test_obj), normalize = TRUE)
```

get_width 13

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Get the width of the segments in each cell type

Description

Get the width of the segments in each cell type

Usage

```
get_width(segments, average = FALSE)
```

Arguments

segments

A GRanges object. Usually the output of calling segment on the the output

object of lean_model.

average

A logical. Whether the width should be averaged across cells.

Value

A data.frame

Examples

```
get_width(segment(test_obj))
get_width(segment(test_obj), average = TRUE)
```

learn_model

Learn a multi-state model from chromatin data

Description

Integrate multiple ChIP-seq chromatin datasets of histone modifications, transcription factors or other DNA binding proteins to build a multi-state model of the combinatorial and spatial frequently occurring patterns. The function uses as an input binarized ChIP-seq data and the genome annotations on which the states will be discovered.

Usage

```
learn_model(
  inputdir,
  outputdir,
  numstates,
  coordsdir,
  anchorsdir,
  chromsizefile,
```

14 learn_model

```
assembly,
cells,
annotation,
binsize,
inputbamdir,
cellmarkfiletable,
read_only = FALSE,
read_bins = FALSE,
counts = FALSE
```

Arguments

inputdir A string. The path to binarized files.

outputdir A string. The path to a directory where output will be written.

numstates An integer. The number of desired states in the model.

coordsdir A string. The path to genomic coordinates files.

anchorsdir A string. The path to the genomic anchors files.

chromsizefile A string. The path to the chromosomes sizes file.

A string. The name of the genomic assembly.

cells A character vector. The names of the cells as they occur in the binarized files

(first line).

annotation A string. The name of the type of annotation as it occurs in the genomic anno-

tation files.

binsize An integer. The number in bp used to generate binarized files.

inputbamdir A string. The path to the input bam files. Only used when count = TRUE.

cellmarkfiletable

A string. The path to the input files table. Only used when bins = TRUE.

read_only A logical. Default is FALSE. Whether to look for and load output files or generate

the model from scratch.

read_bins A logical. Default is FALSE. Whether to load the binarized data into the output

object.

counts A logical. Default is FALSE. Whether to load the reads counts in bins data into

the output object.

Details

By default, this functions runs the analysis commands, writes the output to files and loads it into an object of class segmentation. In addition, the binarized data and the reads counts in the bins can be loaded. When read_only is TRUE. The functions looks for previously generated files in the output directory and load them without rerunning the commands.

Value

An object of class segmentation (see for details) and the files written to the output directory.

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See Also

LearnModel

Examples

```
# locate input and output files
inputdir <- system.file('extdata/SAMPLEDATA_HG18',</pre>
                         package = 'segmenter')
outputdir <- tempdir()</pre>
coordsdir <- system.file('extdata/COORDS',</pre>
                          package = 'chromhmmData')
anchorsdir <- system.file('extdata/ANCHORFILES',</pre>
                            package = 'chromhmmData')
chromsizefile <- system.file('extdata/CHROMSIZES',</pre>
                               'hg18.txt',
                               package = 'chromhmmData')
# run command
obj <- learn_model(inputdir = inputdir,</pre>
                    outputdir = outputdir,
                    coordsdir = coordsdir,
                    anchorsdir = anchorsdir,
                    chromsizefile = chromsizefile,
                    numstates = 3,
                    assembly = 'hg18',
                    cells = c('K562', 'GM12878'),
                    annotation = 'RefSeq',
                    binsize = 200)
# show the output
obj
```

merge_segments_bins

Merge segments and bins objects

Description

Merge segments and bins objects

Usage

```
merge_segments_bins(segments, bins)
```

Arguments

segments A GRanges object. Usually the output of calling segment on the the output

object of lean_model.

bins A SummarizedExperiment object. Usually the output of calling bins on the the

output object of lean_model.

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Value

A SummarizedExperiment object with the segment assignment added to the metadata of the rowRanges.

methods

Methods to interact with segmentation objects

Description

These functions can be used to interact with segmentation objects for purposes other than accessing or modifying their contents.

Usage

```
## S4 method for signature 'segmentation'
show(object)
```

Arguments

object

An object of class segmentation

Value

Prints a summary of the segmentation object contents.

See Also

segmentation accessors

Examples

```
show(test_obj)
```

model_file

Make model file name

Description

Make model file name

Usage

```
model_file(numstates)
```

overlap_files 17

Arguments

numstates An integer

Value

A string

Examples

```
model_file(3)
```

overlap_files

Make overlap file names

Description

Make overlap file names

Usage

```
overlap_files(numstates, cells)
```

Arguments

numstates An integer

cells A character vector

Value

A character vector

```
overlap_files(3, 'K562')
```

range_bins

plot_heatmap	Visualize the model output
--------------	----------------------------

Description

Visualize the model output

Usage

```
plot_heatmap(obj, type = "emission", ...)
```

Arguments

obj A segmentation object

type A string. Which kind of parameter to print. Default is 'emission' and possible

values are 'emission', 'transition', 'overlap', 'TSS' or 'TES'

. . . Other arguments to path to Heatmap

Value

A heatmap

Examples

```
plot_heatmap(test_obj)
```

range_bins	Format the loaded binarized data	
------------	----------------------------------	--

Description

The function takes the data. frames of the loaded binarized data files and format them into GRanges or SummarizedExperiment objects.

Usage

```
range_bins(bins, chromsizefile, binsize, return = "GRanges", tidy = TRUE)
```

Arguments

bins A list of the read_bins_file output.

chromsizefile A string. The path to the chromosomes sizes file.

binsize An integer. The number in bp used to generate binarized files.

return A string. Possible values are GRanges (default) or SummarizedExperiment.
tidy A logical. Default is TRUE. Whether to tidy the metadata columns of the

GRanges object.

range_counts 19

Value

 ${\tt GRanges} \ (default) \ or \ {\tt SummarizedExperiment}.$

range_counts	Format the loaded counts data
3-1-1-1	

Description

The function takes the data.frames of the loaded counts data and format them into GRanges or SummarizedExperiment objects.

Usage

```
range_counts(
  counts,
  features,
  return = "GRanges",
  tidy = FALSE,
  average = FALSE,
  marks
)
```

Arguments

counts	A matrix of the read_bam_file output.
features	A GRanges. That was used to count the bam files.
return	$A\ string.\ Possible\ values\ are\ {\tt GRanges}\ (default)\ or\ {\tt SummarizedExperiment}.$
tidy	A logical. Default is TRUE. Whether to tidy the metadata columns of the $\ensuremath{GRanges}$ object.
average	A logical. Default is FALSE. Whether to average the counts by marks before building the object.
marks	A character vector. The length shoul equal the numbe of columns in counts and is used for averaging and renaming the matrix columns.

Value

GRanges (default) or SummarizedExperiment.

20 read_bins_file

read_bam_file

Read bam files

Description

Count the reads in each range of the GRanges object

Usage

```
read_bam_file(file, features, ...)
```

Arguments

file A string. The path to the file.

features A GRanges object.

... Other arguments passed to bamCount.

Value

A matrix

Examples

read_bins_file

Read bins files

Description

The files contain the cell and the chromosome info in the first line and the binarized data from all marks in the rest.

Usage

```
read_bins_file(file)
```

read_cellmark_file 21

Arguments

file

A string. The path to the file.

Value

A list of 3 items: cell, seqname and binaries.

Examples

read_cellmark_file

Read cellmarktable file

Description

The file should contain at least three columns: cell, mark and file for the names of the cells/conditions, the available marks and binarized data files.

Usage

```
read_cellmark_file(file)
```

Arguments

file

A string. The path to the file.

Value

A data.frame

22 read_emissions_file

Description

The file should contain exactly two columns. One for the name of the chromosome and the other for its length.

Usage

```
read_chromsize_file(file)
```

Arguments

file A string. The path to the file.

Value

A data.frame

Examples

Description

The segments files are the output of running learn_model and named emissions_3_segment.bed

Usage

```
read_emissions_file(file, states, marks)
```

Arguments

file A string. The path to the file.

states A character vector. The names of the states.

Marks A character vector. The names of the marks

read_enrichment_file 23

Value

A matrix

Examples

```
# locate the file
fl <- file.path(tempdir(), 'emissions_3.txt')
# read the file
read_emissions_file(fl)</pre>
```

read_enrichment_file Read enrichment files

Description

The segments files are the output of running learn_model and named <cell>_3_TSS.txt or <cell>_3_TES.txt.

Usage

```
read_enrichment_file(file, states, regions)
```

Arguments

file A string. The path to the file.

states A character vector. The names of the states.
regions A character vector. The names of the regions.

Value

Amatrix

```
# locate the file
fl <- file.path(tempdir(), 'GM12878_3_RefSeqTSS_neighborhood.txt')
# read the file
read_enrichment_file(fl)</pre>
```

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read_model_file

Read modelfile

Description

The model file is the output of running learn_model and named model_#.txt

Usage

```
read_model_file(file)
```

Arguments

file

A string. The path to the file.

Value

```
A data.frame
```

Examples

```
# locate the file
modelfile <- file.path(tempdir(), 'model_3.txt')
# read the file
read_model_file(modelfile)</pre>
```

read_overlap_file

Read segments files

Description

The segments files are the output of running learn_model and named <cell>_3_overlap.txt

Usage

```
read_overlap_file(file, states, regions)
```

Arguments

file A string. The path to the file.

states A character vector. The names of the states.
regions A character vector. The names of the regions.

read_segements_file 25

Value

 $A \; \mathsf{matrix}$

Examples

```
# locate the file
fl <- file.path(tempdir(), 'GM12878_3_overlap.txt')
# read the file
read_overlap_file(fl)</pre>
```

read_segements_file Read_segements_file

Read segments *files*

Description

The segments files are the output of running learn_model and named <cell>_3_segment.bed

Usage

```
read_segements_file(file, states)
```

Arguments

file A string. The path to the file.

states A character vector. The names of the states.

Value

A data.frame

```
# locate the file
segmentfile <- file.path(tempdir(), 'GM12878_3_segments.bed')
# read the file
segs <- read_segements_file(segmentfile)
head(segs)</pre>
```

26 segmentation

```
read_transitions_file Read transitions file
```

Description

The segments files are the output of running learn_model and named transitions_3_segment.bed

Usage

```
read_transitions_file(file, states)
```

Arguments

file A string. The path to the file.

states A character vector. The names of the states.

Value

A matrix

Examples

```
# locate the file
fl <- file.path(tempdir(), 'transitions_3.txt')
# read the file
read_transitions_file(fl)</pre>
```

segmentation

segmentation objects

Description

The segmentation class consists of matrices and lists. The components contain the output of the chromatin segmentation analysis. Loading the input data is optional. The object is returned as a result of calling learn_model or reading its already existing output.

Slots

model list. The list consists of 6 items corresponding to the contents of the model_#.txt file. These are number_states and number_marks for the numbers of states and marks in the model; likelihood and probinit for the likelihood and the initial probabilities of the multistate model; transitionprobs and emissionprobs for the probabilities of the transitions and emissions parameters of the model. Can be accessed using model.

segments_files 27

emission matrix. The matrix contains the emission parameters of n states (rows) for n marks (columns) corresponding to the contents of the emission_#.txt file. Can be accessed using emission.

- transition matrix. The matrix contains the transition parameters of n by n states corresponding to the contents of the transition_#.txt file. Can be accessed using transition.
- overlap list. A list of n number of cells/conditions items. Each item is a matrix of the overlap enrichment of n states (rows) at n genomic annotations (columns) corresponding to the contents of the <cell>_#_overlap.txt files. Can be accessed using overlap.
- TSS list. A list of n number of cells/conditions items. Each item is a matrix of the overlap enrichment of n states (rows) at n locations around the transcription start site (TSS) (columns) corresponding to the contents of the <cell>_#_TSS_neighborhood.txt files. Can be accessed using TSS.
- TES list. A list of n number of cells/conditions items. Each item is a matrix of the overlap enrichment of n states (rows) at n locations around the transcription end site (TES) (columns) corresponding to the contents of the <cell>_#_TES_neighborhood.txt files. Can be accessed using TES.
- segment list. A list of n number of cells/conditions items. Each item is a GRanges object containing the segmentation and assigned states as a metadata column 'state'. These contents correspond to the <cell>_#_segment.bed files. Annotations of the ranges are optional. Can be accessed using segment.
- bins list. A list of n number of cells/conditions items. Each item is a SummarizedExperiment object containing the binarized input data. The coordinates of the bins are saved as the rowRanges each assigned to a state and the binary data itself is saved as assay. Can be accessed using bins.
- counts list. A list of n number of cells/conditions items. Each item is a SummarizedExperiment object containing the read counts in bins. The coordinates of the bins are saved as the rowRanges each assigned to a state and the counts data itself is saved as assay. Can be accessed using counts.

See Also

learn model

segments_files

Make segments file names

Description

Make segments file names

Usage

segments_files(numstates, cells)

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Arguments

numstates An integer

cells A character vector

Value

A character vector

Examples

```
segments_files(3, 'K562')
```

test_obj

A segmentation object generated from the test data

Description

A segmentation object generated by running lean_model on the test dataset in 'inst/extdata/ChromHMM/SAMPLEDATA_He The source code to this run is in 'inst/script/test_obj.R'

Usage

test_obj

Format

An object of class segmentation of length 1.

test_objs

A a list of segmentation objects generated from the test data

Description

A segmentation object generated by running lean_model on the test dataset in 'inst/extdata/ChromHMM/SAMPLEDATA_He for 3 to 8 states. The source code to this run is in 'inst/script/test_objs.R'

Usage

test_objs

Format

An object of class list of length 6.

tidy_ranges 29

tidy_ranges

Tidy the metadata of a GRanges object

Description

Tidy the metadata of a GRanges object

Usage

```
tidy_ranges(gr, columns, low = 0)
```

Arguments

gr A GRanges object

columns A character vectors. The names of columns to be tidied.

low An integer. All values <= this integer will be removed.

Value

A GRanges object

Examples

```
tidy_ranges(segment(test_obj, cell = 'K562')[[1]])
```

transitions_file

Make transitions file name

Description

Make transitions file name

Usage

```
transitions_file(numstates)
```

Arguments

numstates An integer

Value

A string

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Examples

transitions_file(3)

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