Package ‘segmenter’

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Type Package

Title Perform Chromatin Segmentation Analysis in R by Calling ChromHMM

Version 1.8.0

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.

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Depends R (>= 4.1)

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Author Mahmoud Ahmed [aut, cre] (<https://orcid.org/0000-0002-4377-6541>)
Maintainer Mahmoud Ahmed <mahmoud.s.fahmy@students.kasralainy.edu.eg>

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.Binarize

Call Java BinarizeBed

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.
chromsizefile A string. The path to the 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.
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.
assembly  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

Description

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

model(object)

```r
## S4 method for signature 'segmentation'
model(object)
```

emission(object)

```r
## S4 method for signature 'segmentation'
emission(object)
```

transition(object)

```r
## S4 method for signature 'segmentation'
transition(object)
```

overlap(object, ...)

```r
## S4 method for signature 'segmentation'
overlap(object, cell)
```

TSS(object, ...)

```r
## S4 method for signature 'segmentation'
TSS(object, cell)
```

TES(object, ...)

```r
## S4 method for signature 'segmentation'
TES(object, cell)
```

segment(object, ...)

```r
## S4 method for signature 'segmentation'
segment(object, cell)
```

bins(object, ...)

```r
## S4 method for signature 'segmentation'
bins(object, cell)
```

counts(object, ...)

```r
## S4 method for signature 'segmentation'
counts(object, cell)
```

likelihood(object)
## 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

### Examples

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)
TES(test_obj, cell = 'K562')

segment(test_obj)
annotate_segments

    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.

Examples

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)
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
inputdir A string. The directory of the bam files.
cellmarkfiletable 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_bed

Examples
# locate input and output files
inputdir <- system.file("extdata", package = "bamsignals")
cellmarkfiletable <- system.file("extdata",  
  'cell_mark_table.tsv',  
  package = 'segmenter')
chromsizefile <- system.file("extdata/CHROMSIZE",  
  'hg18.txt',  
  package = 'chromhmmData')
outputdir <- tempdir()

# run command
binarize_bed

binarize_bed(inputdir,
    chromsizefile = chromsizefile,
    cellmarkfiletable = cellmarkfiletable,
    outputdir = outputdir)

# show output files
list.files(outputdir, pattern = '*_binary.txt')

---

**binarize_bed**  
*Binarize the bed files*

**Description**

Transform the aligned reads into a binary format.

**Usage**

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

**Arguments**

- **inputdir**  
  A string. The directory of the bam files.

- **cellmarkfiletable**  
  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
### compare_models

**Compare two or more models**

#### Description

Compare two or more models

#### Usage

```r
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

```r
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

```r
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**

**Value**

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

**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
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 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

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

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 learn_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,
assemble, 
cells, 
anotation, 
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.
assembly 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).
anotation A string. The name of the type of annotation as it occurs in the genomic annotation 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.
mergeSegmentsBins

See Also
LearnModel

Examples

# locate input and output files
inputdir <- system.file('extdata/SAMPLEDATA_HG18',
  package = 'segmenter')
outputdir <- tempdir()
coordsdir <- system.file('extdata/COORDS',
  package = 'chromhmmData')
anchorsdir <- system.file('extdata/ANCHORFILES',
  package = 'chromhmmData')
chromsizefile <- system.file('extdata/CHROMSIZES',
  'hg18.txt',
  package = 'chromhmmData')

# run command
obj <- learn_model(inputdir = inputdir,
  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 output object of learn_model.

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

```r
## 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**

```r
show(test_obj)
```

---

**model_file**

*Make model file name*

---

**Description**

Make model file name

**Usage**

```r
model_file(numstates)
```
**overlap_files**

**Arguments**

- **numstates**
  - An integer

**Value**

- A string

**Examples**

```
model_file(3)
```

---

**Description**

Make overlap file names

**Usage**

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

**Arguments**

- **numstates**
  - An integer
- **cells**
  - A character vector

**Value**

- A character vector

**Examples**

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

**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**

```r
plot_heatmap(test_obj)
```
range_counts

Value

GRanges (default) or SummarizedExperiment.

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 GRanges (default) or SummarizedExperiment.
tidy A logical. Default is TRUE. Whether to tidy the metadata columns of the 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 should equal the number of columns in counts and is used for averaging and renaming the matrix columns.

Value

GRanges (default) or SummarizedExperiment.
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

# locate the bam file
bam_file <- system.file("extdata", "randomBam.bam", package = "bamsignals")

# load a granges object
rand_anno <- system.file("extdata",
    "randomAnnot.Rdata",
    package = "bamsignals")
features <- GenomicRanges::promoters(get(load(rand_anno)))

# count reads in ranges
read_bam_file(bam_file, features)

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

**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**

```r
read_cellmark_file(file)
```

**Arguments**

- `file`  
  A string. The path to the file.

**Value**

A data.frame

**Examples**

```r
# locate the file
fl <- system.file('extdata/SAMPLEDATA_HG18/',
                  'GM12878_chr11_binary.txt.gz',
                  package = 'segmenter')

# read the file
read_bins_file(fl)
```

---

```r
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**

```r
read_cellmark_file(file)
```

**Arguments**

- `file`  
  A string. The path to the file.

**Value**

A data.frame

**Examples**

```r
# locate the file
fl <- system.file('extdata',
                  'cell_mark_table.tsv',
                  package = 'segmenter')

# read the file
read_cellmark_file(fl)
```
read_chromsize_file  Read chromsize 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
# locate the file
cchromsizefile <- system.file('extdata/CHROMIZES',
                           'hg18.txt',
                           package = 'chromhmmData')

# read the file
read_chromsize_file(chromsizefile)

read_emissions_file  Read emissions file

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

Value
A matrix

Examples
# locate the file
fl <- file.path(tempdir(), 'emissions_3.txt')

# read the file
read_emissions_file(fl)

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
A matrix

Examples
# locate the file
fl <- file.path(tempdir(), 'GM12878_3_RefSeqTSS_neighborhood.txt')

# read the file
read_enrichment_file(fl)
read_model_file  Read model file

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)

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.
Value
A matrix

Examples

# locate the file
fl <- file.path(tempdir(), 'GM12878_3_overlap.txt')

# read the file
read_overlap_file(fl)

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

Examples

# locate the file
segmentfile <- file.path(tempdir(), 'GM12878_3_segments.bed')

# read the file
segs <- read_segements_file(segmentfile)
head(segs)
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)

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 multi-state model; transitionprobs and emissionprobs for the probabilities of the transitions and emissions parameters of the model. Can be accessed using model.
segments_files

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

Description

Make segments file names

Usage

segments_files(numstates, cells)
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_HG18`. 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 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_HG18` 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  

Tidy the metadata of a GRanges object

Description

Tidy the metadata of a GRanges object

Usage

```r
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

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

transitions_file  

Make transitions file name

Description

Make transitions file name

Usage

```r
transitions_file(numstates)
```

Arguments

- `numstates`: An integer

Value

A string
Examples

transitions_file(3)
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