

Package ‘periodicDNA’

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Type Package

Title Set of tools to identify periodic occurrences of k-mers in DNA sequences

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Description This R package helps the user identify k-mers (e.g. di- or tri-nucleotides) present periodically in a set of genomic loci (typically regulatory elements). The functions of this package provide a straightforward approach to find periodic occurrences of k-mers in DNA sequences, such as regulatory elements. It is not aimed at identifying motifs separated by a conserved distance; for this type of analysis, please visit MEME website.

URL <https://github.com/js2264/periodicDNA>

BugReports <https://github.com/js2264/periodicDNA/issues>

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Depends R (>= 4.0), Biostrings, GenomicRanges, IRanges, BSgenome, BiocParallel

Imports S4Vectors, rtracklayer, stats, GenomeInfoDb, magrittr, zoo, ggplot2, methods, parallel, cowplot

Suggests BSgenome.Scerevisiae.UCSC.sacCer3, BSgenome.Celegans.UCSC.ce11, BSgenome.Dmelanogaster.UCSC.dm6, BSgenome.Drerio.UCSC.danRer10, BSgenome.Hsapiens.UCSC.hg38, BSgenome.Mmusculus.UCSC.mm10, reticulate, testthat, covr, knitr, rmarkdown, pkgdown

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ce11_all_REs	<i>ce11_all_REs</i>
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Description

Regulatory elements annotated in *C. elegans* (ce11) according to Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv.

Usage

```
data(ce11_all_REs)
```

Format

GRanges

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv. ([DOI](#))

Examples

```
data(ce11_all_REs)
table(ce11_all_REs$regulatory_class)
table(ce11_all_REs$which.tissues)
```

ce11_ATACseq	<i>ce11_ATACseq</i>
--------------	---------------------

Description

Sample of ATAC-seq from mixed tissues in *C. elegans* young adults

Usage

```
data(ce11_ATACseq)
```

Format

RleList

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv. ([DOI](#))

Examples

```
data(ce11_ATACseq)
ce11_ATACseq
```

ce11_proms

ce11_proms

Description

Promoters annotated in *C. elegans* (ce11) according to Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv.

Usage

```
data(ce11_proms)
```

Format

GRanges

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv. ([DOI](#))

Examples

```
data(ce11_proms)
table(ce11_proms$which.tissues)
```

ce11_proms_seqs

ce11_proms_seqs

Description

Sample of sequences of promoters annotated in *C. elegans* (ce11) according to Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv.

Usage

```
data(ce11_proms_seqs)
```

Format

DNASTringSet

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv. ([DOI](#))

Examples

```
data(ce11_proms_seqs)
head(ce11_proms_seqs)
```

ce11_TSSs

ce11_TSSs

Description

Coordinates of promoter TSSs annotated in *C. elegans* (ce11) used in Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv.

Usage

```
data(ce11_TSSs)
```

Format

GRanges

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", BiorXiv. ([DOI](#))

Examples

```
data(ce11_TSSs)
lengths(ce11_TSSs)
ce11_TSSs[[1]]
```

`ce11_WW_10bp``ce11_WW_10bp`

Description

Sample of WW 10-bp periodicity track generated by `getPeriodicityTrack()` in `ce11` over annotated accessible sites, with default parameters

Usage

```
data(ce11_WW_10bp)
```

Format

RleList

Source

[BiorXiv](#)

References

Serizay et al. 2020, "Tissue-specific profiling reveals distinctive regulatory architectures for ubiquitous, germline and somatic genes", [BiorXiv](#). ([DOI](#))

Examples

```
data(ce11_WW_10bp)
ce11_WW_10bp
```

`getPeriodicity``A function to compute k-mer periodicity in sequence(s).`

Description

This function takes a set of sequences and a k-mer of interest, map a k-mer of interest in these sequences, computes all the pairwise distances (distogram), normalize it for distance decay, and computes the resulting power spectral density of the normalized distogram.

Usage

```

getPeriodicity(x, motif, ...)

## S3 method for class 'DNAStrngSet'
getPeriodicity(
  x,
  motif,
  range_spectrum = seq(1, 200),
  BPPARAM = setUpBPPARAM(1),
  roll = 3,
  verbose = TRUE,
  sample = 0,
  n_shuffling = 0,
  cores_shuffling = 1,
  cores_computing = 1,
  order = 1,
  ...
)

## S3 method for class 'GRanges'
getPeriodicity(x, motif, genome = "BSgenome.Celegans.UCSC.ce11", ...)

## S3 method for class 'DNAStrng'
getPeriodicity(x, motif, ...)

```

Arguments

<code>x</code>	a DNAStrng, DNAStrngSet or GRanges object.
<code>motif</code>	a k-mer of interest
<code>...</code>	Arguments passed to S3 methods
<code>range_spectrum</code>	Numeric vector Range of the distogram to use to run the Fast Fourier Transform on (default: 1:200, i.e. all pairs of k-mers at a maximum of 200 bp from each other).
<code>BPPARAM</code>	split the workload over several processors using BiocParallel
<code>roll</code>	Integer Window to smooth the distribution of pairwise distances (default: 3, to discard the 3-bp periodicity of dinucleotides which can be very strong in vertebrate genomes)
<code>verbose</code>	Boolean
<code>sample</code>	Integer if > 0, will randomly sample this many integers from the dists vector before normalization. This ensures consistency when looking at periodicity in different genomes, since different genomes will have different GC percent
<code>n_shuffling</code>	Integer, how many times should the sequences be shuffled? (default = 0)
<code>cores_shuffling</code>	integer, Number of cores used for shuffling (used if n_shuffling > 0)

cores_computing	integer, split the workload over several processors using BiocParallel (used if n_shuffling > 0)
order	Integer, which order to take into consideration for shuffling (ushuffle python library must be installed for orders > 1) (used if n_shuffling > 0)
genome	genome ID, BSgenome or DNASTringSet object (optional, if x is a GRanges)

Value

A list containing the results of getPeriodicity function.

- The dists vector is the raw vector of all distances between any possible k-mer.
- The hist data.frame is the distribution of distances over range_spectrum.
- The normalized_hist is the raw hist, normalized for decay over increasing distances.
- The spectra object is the output of the FFT applied over normalized_hist.
- The PSD data frame is the power spectral density scores over given frequencies.
- The motif object is the k-mer being analysed.
- The final periodicity metrics computed by getPeriodicity()

If getPeriodicity() is ran with n_shuffling > 0, the resulting list also contains PSD values computed when iterating through shuffled sequences.

Methods (by class)

- DNASTringSet: S3 method for DNASTringSet
- GRanges: S3 method for GRanges
- DNASTring: S3 method for DNASTring

Examples

```
data(ce11_proms_seqs)
periodicity_result <- getPeriodicity(
  ce11_proms_seqs[1:100],
  motif = 'TT'
)
head(periodicity_result$PSD)
plotPeriodicityResults(periodicity_result)
#
data(ce11_TSSs)
periodicity_result <- getPeriodicity(
  ce11_TSSs[['Ubiq. ']][1:10],
  motif = 'TT',
  genome = 'BSgenome.Celegans.UCSC.ce11'
)
head(periodicity_result$PSD)
plotPeriodicityResults(periodicity_result)
#
data(ce11_TSSs)
periodicity_result <- getPeriodicity(
```



```

    ce11_TSSs[['Ubiq.']] [1:10],
    motif = 'TT',
    genome = 'BSgenome.Celegans.UCSC.ce11',
    n_shuffling = 10
)
head(periodicity_result$PSD)
plotPeriodicityResults(periodicity_result)

```

getPeriodicityTrack *Function to generate a k-mer periodicity track*

Description

This function takes a set of GRanges in a genome, recover the corresponding sequences and divides them using a sliding window. For each sub-sequence, it then computes the PSD value of a k-mer of interest at a chosen period, and generates a linear .bigWig track from these values.

Usage

```

getPeriodicityTrack(
  genome = NULL,
  granges,
  motif = "WW",
  period = 10,
  BPPARAM = setUpBPPARAM(1),
  extension = 1000,
  window_size = 100,
  step_size = 2,
  range_spectrum = seq(5, 50),
  smooth_track = 20,
  bw_file = NULL
)

```

Arguments

genome	DNAStringSet, BSgenome or genome ID
granges	GRanges object
motif	character, k-mer of interest.
period	Integer, the period of the k-mer to study (default=10).
BPPARAM	split the workload over several processors using BiocParallel
extension	Integer, the width the GRanges are going to be extended to (default 1000).
window_size	Integer, the width of the bins to split the GRanges objects in (default 100).
step_size	Integer, the increment between bins over GRanges (default 2).
range_spectrum	Numeric vector, the distances between nucleotides to take into consideration when performing Fast Fourier Transform (default seq_len(50)).
smooth_track	Integer, smooth the resulting track
bw_file	character, the name of the output bigWig track

Value

Rlelist and a bigWig track in the working directory.

Examples

```
data(ce11_proms)
track <- getPeriodicityTrack(
  genome = 'BSgenome.Celegans.UCSC.ce11',
  ce11_proms[1],
  extension = 200,
  window_size = 100,
  step_size = 10,
  smooth_track = 1,
  motif = 'WW',
  period = 10,
  BPPARAM = setUpBPPARAM(1)
)
track
unlink(
  'BSgenome.Celegans.UCSC.ce11_WW_10-bp-periodicity_g-100^10_smooth-1.bw'
)
```

getPeriodicityWithIterations

A function to compute PSDs with iterations

Description

This function computes PSD values of a given k-mer of interest in a set of input sequences. It also iterates the PSD calculation process over shuffled sequences, if `n_shuffling` is used.

Usage

```
getPeriodicityWithIterations(x, ...)

## S3 method for class 'DNAStringSet'
getPeriodicityWithIterations(
  x,
  motif,
  n_shuffling = 10,
  cores_shuffling = 1,
  cores_computing = 1,
  order = 1,
  verbose = 1,
  ...
)

## S3 method for class 'GRanges'
getPeriodicityWithIterations(x, genome, ...)
```

Arguments

x	DNAStringSet, sequences of interest
...	Arguments passed to S3 methods
motif	character, k-mer of interest
n_shuffling	integer, Number of shuffling
cores_shuffling	integer, Number of cores used for shuffling
cores_computing	integer, split the workload over several processors using BiocParallel
order	Integer, which order to take into consideration for shuffling (ushuffle python library must be installed for orders > 1)
verbose	integer, Should the function be verbose?
genome	genome ID, BSgenome or DNAStringSet object (optional, if x is a GRanges)

Value

Several metrics

Methods (by class)

- DNAStringSet: S3 method for DNAString
- GRanges: S3 method for GRanges

Examples

```
data(ce11_proms_seqs)
res <- getPeriodicityWithIterations(
  ce11_proms_seqs[1:10],
  genome = 'BSgenome.Celegans.UCSC.ce11',
  motif = 'TT',
  cores_shuffling = 1
)
res$observed_PSD
res$shuffled_PSD
```

plotAggregateCoverage *A function to plot aggregated signals over sets of GRanges*

Description

This function takes one or several RleList genomic tracks (e.g. imported by rtraklayer::import(..., as = 'Rle')) and one or several GRanges objects. It computes coverage of the GRanges by the genomic tracks and returns an aggregate coverage plot.

Usage

```
plotAggregateCoverage(x, ...)  
  
## S3 method for class 'CompressedRleList'  
plotAggregateCoverage(x, granges, ...)  
  
## S3 method for class 'SimpleRleList'  
plotAggregateCoverage(  
  x,  
  granges,  
  colors = NULL,  
  xlab = "Center of elements",  
  ylab = "Score",  
  xlim = NULL,  
  ylim = NULL,  
  quartiles = c(0.025, 0.975),  
  verbose = FALSE,  
  bin = 1,  
  plot_central = TRUE,  
  run_in_parallel = FALSE,  
  split_by_granges = FALSE,  
  norm = "none",  
  ...  
)  
  
## S3 method for class 'list'  
plotAggregateCoverage(  
  x,  
  granges,  
  colors = NULL,  
  xlab = "Center of elements",  
  ylab = "Score",  
  xlim = NULL,  
  ylim = NULL,  
  quartiles = c(0.025, 0.975),  
  verbose = FALSE,  
  bin = 1,  
  plot_central = TRUE,  
  split_by_granges = TRUE,  
  split_by_track = FALSE,  
  free_scales = FALSE,  
  run_in_parallel = FALSE,  
  norm = "none",  
  ...  
)
```

Arguments

<code>x</code>	a single signal track (<code>CompressedRleList</code> or <code>SimpleRleList</code> class), or several signal tracks (<code>SimpleRleList</code> or <code>CompressedRleList</code> class) grouped in a named list
<code>...</code>	additional parameters
<code>granges</code>	a <code>GRanges</code> object or a named list of <code>GRanges</code>
<code>colors</code>	a vector of colors
<code>xlab</code>	x axis label
<code>ylab</code>	y axis label
<code>xlim</code>	y axis limits
<code>ylim</code>	y axis limits
<code>quartiles</code>	Which quantiles to use to determine y scale automatically?
<code>verbose</code>	Boolean
<code>bin</code>	Integer Width of the window to use to smooth values by <code>zoo::rollMean</code>
<code>plot_central</code>	Boolean Draw a vertical line at 0
<code>run_in_parallel</code>	Boolean Should the plots be computed in parallel using <code>mclapply</code> ?
<code>split_by_granges</code>	Boolean Facet plots over the sets of <code>GRanges</code>
<code>norm</code>	character Should the signal be normalized ('none', 'zscore' or 'log2')?
<code>split_by_track</code>	Boolean Facet plots by the sets of signal tracks
<code>free_scales</code>	Boolean Should each facet have independent y-axis scales?

Value

An aggregate coverage plot.

Methods (by class)

- `CompressedRleList`: S3 method for `CompressedRleList`
- `SimpleRleList`: S3 method for `SimpleRleList`
- `list`: S3 method for list

Examples

```
data(ce11_ATACseq)
data(ce11_WW_10bp)
data(ce11_proms)

p1 <- plotAggregateCoverage(
  ce11_ATACseq,
  resize(ce11_proms[1:100], fix = 'center', width = 1000)
)
p1
```

```

proms <- resize(ce11_proms[1:100], fix = 'center', width = 400)
p2 <- plotAggregateCoverage(
  ce11_ATACseq,
  list(
    'Ubiq & Germline promoters' =
      proms[proms$which.tissues %in% c('Ubiq.', 'Germline')],
    'Other promoters' =
      proms[!(proms$which.tissues %in% c('Ubiq.', 'Germline'))]
  )
)
p2

p3 <- plotAggregateCoverage(
  list(
    'atac' = ce11_ATACseq,
    'WW_10bp' = ce11_WW_10bp
  ),
  proms,
  norm = 'zscore'
)
p3

p4 <- plotAggregateCoverage(
  list(
    'ATAC-seq' = ce11_ATACseq,
    'WW 10-bp periodicity' = ce11_WW_10bp
  ),
  list(
    'Ubiq & Germline promoters' =
      proms[proms$which.tissues %in% c('Ubiq.', 'Germline')],
    'Other promoters' =
      proms[!(proms$which.tissues %in% c('Ubiq.', 'Germline'))]
  ),
  norm = 'zscore'
)
p4

p5 <- plotAggregateCoverage(
  list(
    'ATAC-seq' = ce11_ATACseq,
    'WW 10-bp periodicity' = ce11_WW_10bp
  ),
  list(
    'Ubiq & Germline promoters' =
      proms[proms$which.tissues %in% c('Ubiq.', 'Germline')],
    'Other promoters' =
      proms[!(proms$which.tissues %in% c('Ubiq.', 'Germline'))]
  ),
  split_by_granges = FALSE,
  split_by_track = TRUE,
  norm = 'zscore'
)

```

p5

plotPeriodicityResults

Plot the output of getPeriodicity()

Description

This function plots some results from the result of `getPeriodicity()`. It plots the raw histogram, the distance-decay normalized histogram and the resulting PSD values. If a shuffled control has been performed by `getPeriodicity()`, it also displays it.

Usage

```
plotPeriodicityResults(
  results,
  periods = c(2, 20),
  filter_periods = TRUE,
  facet_control = TRUE,
  xlim = NULL,
  fdr_threshold = 0.05,
  ...
)
```

Arguments

<code>results</code>	The output of <code>getPeriodicity</code> function.
<code>periods</code>	Vector a numerical vector of length 2, to specify the x-axis limits
<code>filter_periods</code>	Boolean Should the x-axis be constrained to the periods?
<code>facet_control</code>	Boolean should the shuffling plots be faceted?
<code>xlim</code>	Integer x axis upper limit in raw and norm. histograms
<code>fdr_threshold</code>	Float, significance threshold
<code>...</code>	Additional theme arguments passed to <code>theme_ggplot2()</code>

Value

list A list containing four ggplots

Examples

```
data(ce11_TSSs)
periodicity_result <- getPeriodicity(
  ce11_TSSs[['Ubiq.']] [1:100],
  genome = 'BSgenome.Celegans.UCSC.ce11',
  motif = 'TT',
  BPPARAM = setUpBPPARAM(1)
```

```

)
head(periodicity_result$PSD)
plotPeriodicityResults(periodicity_result)
plotPeriodicityResults(periodicity_result, xlim = 150)
plotPeriodicityResults(
  periodicity_result, xlim = 150, filter_periods = FALSE
)
plotPeriodicityResults(
  periodicity_result, xlim = 150, facet_control = FALSE
)

```

 setUpBPPARAM

setUpBPPARAM

Description

A function to dynamically select MulticoreParam or SnowParam (if Windows)

Usage

```
setUpBPPARAM(nproc = 1)
```

Arguments

nproc number of processors

Value

A BPPARAM object

Examples

```
BPPARAM <- setUpBPPARAM(1)
```

 theme_ggplot2

Personal ggplot2 theming function, adapted from roboto-condensed at <https://github.com/hrbrmstr/hrbrthemes/>

Description

Personal ggplot2 theming function, adapted from roboto-condensed at <https://github.com/hrbrmstr/hrbrthemes/>

Usage

```

theme_ggplot2(
  grid = TRUE,
  border = TRUE,
  base_size = 8,
  plot_title_size = 12,
  plot_title_face = "plain",
  plot_title_margin = 5,
  subtitle_size = 11,
  subtitle_face = "plain",
  subtitle_margin = 5,
  strip_text_size = 10,
  strip_text_face = "bold",
  caption_size = 9,
  caption_face = "plain",
  caption_margin = 3,
  axis_text_size = base_size,
  axis_title_size = 9,
  axis_title_face = "plain",
  axis_title_just = "rt",
  panel_spacing = grid::unit(2, "lines"),
  grid_col = "#cccccc",
  plot_margin = margin(12, 12, 12, 12),
  axis_col = "#cccccc",
  axis = FALSE,
  ticks = FALSE
)

```

Arguments

grid	panel grid ('TRUE', 'FALSE', or a combination of 'X', 'x', 'Y', 'y')
border	border if 'TRUE' add border
base_size	base font size
plot_title_size, plot_title_margin,	plot title size and margin
plot_title_face,	plot title face
subtitle_face, subtitle_size	plot subtitle face and size
subtitle_margin	plot subtitle margin bottom (single numeric value)
strip_text_face, strip_text_size	facet label font face and size
caption_face, caption_size, caption_margin	plot caption face, size and margin
axis_text_size	font size of axis text

<code>axis_title_face</code> , <code>axis_title_size</code>	axis title font face and size
<code>axis_title_just</code>	axis title font justificationk one of <code>'[blmcr]'</code>
<code>panel_spacing</code>	panel spacing (use <code>'unit()'</code>)
<code>grid_col</code>	grid color
<code>plot_margin</code>	plot margin (specify with <code>[ggplot2::margin]</code>)
<code>axis_col</code>	axis color
<code>axis</code>	add x or y axes? <code>'TRUE'</code> , <code>'FALSE'</code> , <code>"xy"</code>
<code>ticks</code>	ticks if <code>'TRUE'</code> add ticks

Value

theme A ggplot theme

Examples

```
library(ggplot2)

ggplot(mtcars, aes(mpg, wt)) +
  geom_point() +
  labs(x="Fuel efficiency (mpg)", y="Weight (tons)",
       title="Seminal ggplot2 scatterplot example") +
  theme_ggplot2()
```

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