Package ‘PWMEnrich’

January 13, 2024

Type Package
Title PWM enrichment analysis
Version 4.38.0
Date 2015-09-25
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LazyLoad yes
Description A toolkit of high-level functions for DNA motif scanning and enrichment analysis built upon Biostrings. The main functionality is PWM enrichment analysis of already known PWMs (e.g. from databases such as MotifDb), but the package also implements high-level functions for PWM scanning and visualisation. The package does not perform ‘`de novo’’ motif discovery, but is instead focused on using motifs that are either experimentally derived or computationally constructed by other tools.
License LGPL (>= 2)
Depends R (>= 3.5.0), methods, BiocGenerics, Biostrings
Imports grid, seqLogo, gdata, evd, S4Vectors
Suggests MotifDb, BSgenome, BSgenome.Dmelanogaster.UCSC.dm3, PWMEnrich.Dmelanogaster.background, testthat, gtools, parallel, PWMEnrich.Hsapiens.background, PWMEnrich.Musculus.background, BiocStyle, knitr
biocViews MotifAnnotation, SequenceMatching, Software
VignetteBuilder knitr
RoxygenNote 7.1.1
Encoding UTF-8
git_url https://git.bioconductor.org/packages/PWMEnrich
git_branch RELEASE_3_18
git_last_commit 5c2bd63
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Description

A toolkit of high-level functions for DNA motif scanning and enrichment analysis built upon Biostrings. The main functionality is PWM enrichment analysis of already known PWMs (e.g. from databases such as MotifDb), but the package also implements high-level functions for PWM scanning and visualisation. The package does not perform "de novo" motif discovery, but is instead focused on using motifs that are either experimentally derived or computationally constructed by other tools.

.inputParamMotifs

Description

Normalizes the motifs input argument for multiple functions

Usage

.inputParamMotifs(motifs)

Arguments

motifs a list of motifs either as frequency matrices (PFM) or as PWM objects. If PFMs are specified they are converted to PWMs using uniform background.
.inputParamSequences Normalize the sequences input argument

**Description**

Normalize the sequences input argument

**Usage**

.inputParamSequences(sequences)

**Arguments**

sequences a set of sequences to be scanned, a list of DNASTring or other scannable objects

---

.inputPFMfromMatrixOrPWM

*Check the frequency matrix input parameter for motifSimilarity*

**Description**

Check the frequency matrix input parameter for motifSimilarity

**Usage**

.inputPFMfromMatrixOrPWM(m)

**Arguments**

m either a PWM object or a matrix

**Value**

corresponding PFM
.normalize.bg.seq  
check consistency of bg.seq input parameter

Description
check consistency of bg.seq input parameter

Usage
.normalize.bg.seq(bg.seq)

Arguments
bg.seq a set of background sequences, either a list of DNAString object or DNAStringSet object

.normargPfm  
Input parameter normalization for PWMUnscaled

Description
This function is from Biostrings package. A Position Frequency Matrix (PFM) is also represented as an ordinary matrix. Unlike a PWM, it must be of type integer (it will typically be the result of consensusMatrix()).

Usage
.normargPfm(x)

Arguments
x a frequency matrix

.normargPriorParams  
Input parameter normalization function for PWMUnscaled

Description
This function is from Biostrings package

Usage
.normargPriorParams(prior.params)

Arguments
prior.params Typical 'prior.params' vector: c(A=0.25, C=0.25, G=0.25, T=0.25)
affinitySequenceSet

Calculate total affinity over a set of sequences

**Description**

Calculate total affinity over a set of sequences

**Usage**

affinitySequenceSet(scores, seq.len, pwm.len)

**Arguments**

- **scores**: affinity scores for individual sequences
- **seq.len**: lengths of sequences
- **pwm.len**: lengths of PWMs

---

as.data.frame,MotifEnrichmentReport-method

Convert a MotifEnrichmentReport into a data.frame object

**Description**

Convert a MotifEnrichmentReport into a data.frame object

**Usage**

```r
## S4 method for signature 'MotifEnrichmentReport'
as.data.frame(x, row.names = NULL, optional = FALSE, ...)
```

**Arguments**

- **x**: the MotifEnrichmentReport object
- **row.names**, **optional**, **...**: unused
Calculate the Clover P-value as described in the Clover paper

Description

This function only take one background sequence as input, it also just calculates the P-value so it is more efficient.

Usage

cloverPvalue1seq(
    scores,
    seq.len,
    pwm.len,
    bg.fwd,
    bg.rev,
    B = 1000,
    verbose = TRUE,
    clover = NULL
)

Arguments

scores the affinity scores for individual sequences
seq.len lengths of sequences
pwm.len lengths of PWMs
bg.fwd the raw score of forward strand
bg.rev the raw scores of reverse strand
B the number of random replicates
verbose if to give verbose progress reports
clover the clover scores if already calculated

Value

P-value
cloverScore

Calculate the Clover score using the recursive formula from Frith et al

Description

Calculate the Clover score using the recursive formula from Frith et al

Usage

cloverScore(scores, lr3 = FALSE, verbose = FALSE)

Arguments

scores a matrix of average odds scores, where columns are motifs, and rows sequences
lr3 if to return a matrix of LR3 scores, where columns correspond to motifs, and rows to subset sizes
verbose if to produce verbose output of progress

Value

the LR4 score, which is the mean of LR3 scores over subset sizes

colMedians

Calculate medians of columns

Description

Calculate medians of columns

Usage

colMedians(x)

Arguments

x a matrix
colSds  
*Calculate standard deviations of columns*

**Description**

Calculate standard deviations of columns

**Usage**

`colSds(x)`

**Arguments**

- `x`  a matrix

---

concatenateSequences  
*Concatenate DNA sequences into a single character object*

**Description**

Concatenate DNA sequences into a single character object

**Usage**

`concatenateSequences(sequences)`

**Arguments**

- `sequences`  either a list of DNAString objects, or a DNAStringSet

**Value**

- a single character string
cutoffZscore

Z-score calculation for cutoff hits

Description

The Z-score is calculated separately for each sequence

Usage

cutoffZscore(scores, seq.len, pwm.len, bg.P)

Arguments

scores  the hit counts for the sequences
seq.len  the length distribution of sequences
pwm.len  the length distribution of the PWMs
bg.P    background probabilities of observing a motif hit at nucleotide resolution (scaled to sequence length, not 2 * length)

Value

Z-score

cutoffZscoreSequenceSet

Z-score calculation for cutoff hits for group of sequences

Description

The Z-score is calculated as if the sequence came from one very long sequence

Usage

cutoffZscoreSequenceSet(scores, seq.len, pwm.len, bg.P)

Arguments

scores  the hit counts for the sequences
seq.len  the length distribution of sequences
pwm.len  the length distribution of the PWMs
bg.P    background probabilities of observing a motif hit at nucleotide resolution

Value

Z-score
**divideRows**  
*Divide each row of a matrix with a vector*

**Description**

Divide each row of a matrix with a vector

**Usage**

`divideRows(m, v)`

**Arguments**

- `m`  
  matrix to be divided

- `v`  
  the vector to use for division

---

**DNAStringSetToList**  
*Convert DNAStringSet to list of DNAString objects*

**Description**

as.list doesn’t seem to always work for DNAStringSets, so implementing this ourselves.

**Usage**

`DNAStringSetToList(x)`

**Arguments**

- `x`  
  an object of class DNAStringSet

---

**empiricalPvalue**  
*Calculate the empirical P-value by affinity of cutoff.*

**Description**

This is the new backend function for empirical P-values for either affinity or cutoff. The function only works on single sequences.
Usage

```r
empiricalPvalue(
  scores,
  seq.len,
  pwm.len,
  bg.fwd,
  bg.rev,
  cutoff = NULL,
  B = 10000,
  verbose = FALSE,
  exact.length = FALSE
)
```

Arguments

- **scores**: the scores obtained for the sequence
- **seq.len**: the length of the sequence, if a single value will take a single sequence of given length. If a vector of values, will take sequences of given lengths and joint them together
- **pwm.len**: the lengths of PWMs
- **bg.fwd**: raw odds scores for the forward strand of background
- **bg.rev**: raw odds scores for the reverse strand of background
- **cutoff**: if not NULL, will use hit count above this cutoff. The cutoff should be specified in log2.
- **B**: the number of random replicates
- **verbose**: if to give verbose progress reports
- **exact.length**: if to take into consideration that the actual sequence lengths differ for different PWMs. For very long sequences (i.e. seq.len > pwm.len) this make very little difference, however the run time with exact.length is much longer.

Description

Calculate empirical P-value for a set of sequences, using either affinity or cutoff. When cutoff is used, the score is a number of motif hits above a certain log-odds cutoff.
getBackgroundFrequencies

Usage

empiricalPvalueSequenceSet(
  scores,
  seq.len,
  pwm.len,
  bg.fwd,
  bg.rev,
  cutoff = NULL,
  B = 10000,
  verbose = FALSE
)

Arguments

  scores       a matrix of scores, rows for sequences, columns for PWMs
  seq.len      the lengths of sequences
  pwm.len      the lengths of PWMs
  bg.fwd       raw odds scores for the forward strand of background
  bg.rev       raw odds scores for the reverse strand of background
  cutoff       if not NULL, will use hit count above this cutoff. The cutoff should be specified in log2.
  B            the number of random replicates
  verbose      if to give verbose progress reports

getBackgroundFrequencies

Get the four nucleotides background frequencies

Description

Estimate the background frequencies of A,C,G,T on a set of promoters from an organism

Usage

getBackgroundFrequencies(organism = "dm3", pseudo.count = 1, quick = FALSE)

Arguments

  organism     either a name of the organisms for which the background should be compiled
               (supported names are "dm3", "mm9" and "hg19"), a BSgenome object, DNAStringSet,
               or list of DNAString objects
  pseudo.count the number to which the frequencies sum up to, by default 1
  quick         if to preform fitting on a reduced set of 100 promoters. This will not give as
good results but is much quicker than fitting to all the promoters (~10k). Usage of this parameter is recommended only for testing and rough estimates.
getPromoters

Author(s)
Robert Stojnic, Diego Diez

Examples
```r
## Not run:
getBackgroundFrequencies("dm3")
## End(Not run)
```

getPromoters

Get the promoter sequences either for a named organism such as "dm3" or a BSgenome object

Description
Get the promoter sequences either for a named organism such as "dm3" or a BSgenome object

Usage
getPromoters(organismOrGenome)

Arguments
organismOrGenome
either organism name, e.g. "dm3", or BSgenome object

Value
a list of: promoters - DNAStringSet of (unique) promoters; organism - name of species; version - genome version

gevPerSequence

Apply GEV background normalization per every sequence

Description
Apply GEV background normalization per every sequence

Usage
gevPerSequence(scores, seq.len, pwm.len, bg.loc, bg.scale, bg.shape)
Arguments

- **scores**: affinity scores for the PWMs, can contain scores for more than one sequence (as rows), P-values are extracted separately
- **seq.len**: the length distribution of the sequences
- **pwm.len**: the lengths of PWMs
- **bg.loc**: list of linear regression for location parameter
- **bg.scale**: list of linear regression for scale parameter
- **bg.shape**: list of linear regression for shape parameter

**Description**

Generate a motif enrichment report for the whole group of sequences together

**Usage**

```r
## S4 method for signature 'MotifEnrichmentResults'
groupReport(obj, top = 0.05, bg = TRUE, by.top.motifs = FALSE, ...)
```

**Arguments**

- **obj**: a MotifEnrichmentResults object
- **top**: what proportion of top motifs should be examined in each individual sequence (by default 0.05, i.e. 5%)
- **bg**: if to use background corrected P-values to do the ranking (if available)
- **by.top.motifs**: if to rank by the proportion of sequences where the motif is within 'top' percentage of motifs
- **...**: unused

**Value**

A MotifEnrichmentReport object containing a table with the following columns:

- 'rank': The rank of the PWM’s enrichment in the whole group of sequences together
- 'target': The name of the PWM’s target gene, transcript or protein complex.
- 'id': The unique identifier of the PWM (if set during PWM creation).
- 'raw.score': The raw score before P-value calculation
- 'p.value': The P-value of motif enrichment (if available)
- 'top.motif.prop': The proportion (between 0 and 1) of sequences where the motif is within top proportion of enrichment motifs.
```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # load the pre-compiled lognormal background

  # scan two sequences for motif enrichment
  sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                   DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))
  res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)

  # produce a report for all sequences taken together
  r.default = groupReport(res)

  # produce a report where the last column takes top 1% motifs
  r = groupReport(res, top=0.01)

  # view the results
  r

  # plot the top 10 most enriched motifs
  plot(r[1:10])
}
```

---

**keepFinite**

Replace all infinite values by 0

**Description**

Replace all infinite values by 0

**Usage**

```r
keepFinite(x)
```

**Arguments**

- `x`: a vector of values
logNormPval

**Calculate the P-value from lognormal distribution with background of equal length**

**Description**
Calculate the P-value from lognormal distribution with background of equal length

**Usage**

```r
logNormPval(scores, seq.len, pwm.len, bg.mean, bg.sd, bg.len, log = FALSE)
```

**Arguments**

- `scores`: affinity scores for the PWMs, can contain scores for more than one sequence (as rows), P-values are extracted separately
- `seq.len`: the length distribution of the sequences
- `pwm.len`: the lengths of PWMs
- `bg.mean`: the mean values from the background for PWMs
- `bg.sd`: the sd values from the background
- `bg.len`: the length distribution of the background (we currently support only constant length)
- `log`: if to produce log p-values

---

logNormPvalSequenceSet

**Lognormal P-value for a set of sequences**

**Description**
Lognormal P-value for a set of sequences

**Usage**

```r
logNormPvalSequenceSet(scores, seq.len, pwm.len, bg.mean, bg.sd, bg.len)
```

**Arguments**

- `scores`: a matrix of per-sequence affinity scores
- `seq.len`: lengths of sequences
- `pwm.len`: lengths of PWMs
- `bg.mean`: mean background at length of bg.len
- `bg.sd`: standard deviation of background at length of bg.len
- `bg.len`: the length for which mean and sd are calculated
**makeBackground**

**Value**

P-value

---

**Description**

This is a convenience front-end function to compile new backgrounds for a set of PFMs. Currently only supports D. melanogaster, but in the future should support other common organisms as well.

**Usage**

```r
makeBackground(
  motifs,
  organism = "dm3",
  type = "logn",
  quick = FALSE,
  bg.seq = NULL,
  ...
)
```

**Arguments**

- **motifs**: a list of position frequency matrices (4xL matrices)
- **organism**: either a name of the organisms for which the background should be compiled (currently supported names are "dm3", "mm9" and "hg19"), or a BSgenome object (see BSgenome package).
- **type**: the type of background to be compiled. Possible types are:
  - "logn" - estimate a lognormal background
  - "cutoff" - estimate a Z-score background with fixed log-odds cutoff (in log2)
  - "pval" - estimate a Z-score background with a fixed P-value cutoff. Note that this may require a lot of memory since the P-value of motif hits is first estimated from the empirical distribution.
  - "empirical" - create an empirical P-value background. Note that this may require a lot of memory (up to 10GB in default "slow" mode (quick=FALSE) for 126 JASPAR motifs and 1000 D. melanogaster promoters).
  - "GEV" - estimate a generalized extreme value (GEV) distribution background by fitting linear regression to distribution parameters in log space
- **quick**: if to preform fitting on a reduced set of 100 promoters. This will not give as good results but is much quicker than fitting to all the promoters (~10k). Usage of this parameter is recommended only for testing and rough estimates.
- **bg.seq**: a set of background sequences to use. This parameter overrides the "organism" and "quick" parameters.
- **...**: other named parameters that backend function makePWM***Background functions take.
Author(s)

Robert Stojnic, Diego Diez

Examples

# load in the two example de-novo motifs
motifs = readMotifs(system.file(package = "PWMEnrich", dir = "extdata", file = "example.transfac"),
                    remove.acc = TRUE)

## Not run:
# construct lognormal background
bg.logn = makeBackground(motifs, organism="dm3", type="logn")

# alternatively, any BSgenome object can also be used
if(requireNamespace("BSgenome.Dmelanogaster.UCSC.dm3"))
  bg.logn = makeBackground(motifs, organism=Dmelanogaster, type="logn")

# construct a Z-score of hits with P-value background
bg.pval = makeBackground(motifs, organism="dm3", type="pval", p.value=1e-3)

# now we can use them to scan for enrichment in sequences (in this case there is a consensus # Tin binding site).
motifEnrichment(DNAString("TGCATCAAGTGTGTAGTG"), bg.logn)
motifEnrichment(DNAString("TGCATCAAGTGTGTAGTG"), bg.pval)

## End(Not run)

makePriors

Make priors from background sequences

Description

These priors serve both as background nucleotide frequencies and pseudo-counts for PWMs.

Usage

makePriors(bg.seq, bg.pseudo.count)

Arguments

bg.seq a set of background sequences

bg.pseudo.count the total pseudocount shared between nucleotides
Examples

# some example sequences
sequences = list(DNAString("AAAGAGATGACGATGAC"), DNAString("ACGATGAGGATGAC"))
# make priors with pseudo-count of 1 shared between them
makePriors(sequences, 1)

makePWMCutoffBackground

Make a cutoff background

Description

Make a background based on number of motifs hits above a certain threshold.

Usage

makePWMCutoffBackground(
  bg.seq,
  motifs,
  cutoff = log2(exp(4)),
  bg.pseudo.count = 1,
  bg.source = "",
  verbose = TRUE
)

Arguments

bg.seq a set of background sequences, either a list of DNAString object or DNAStringSet object
motifs a set of motifs, either a list of frequency matrices, or a list of PWM objects. If
frequency matrices are given, the background distribution is fitted from bg.seq.
cutoff the cutoff at which the background should be made, i.e. at which a motif hit is
called significant
bg.pseudo.count the pseudo count which is shared between nucleotides when frequency matrices
are given
bg.source a free-form textual description of how the background was generated
verbose if to produce verbose output

Examples

## Not run:
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # make background for MotifDb motifs using 2Kb promoters of all D. melanogaster transcripts
}
# using a cutoff of 5
if(requireNamespace("BSgenome.Dmelanogaster.UCSC.dm3"))
  makePWMCutoffBackground(Dmelanogaster$upstream2000, MotifDb.Dmel.PFM, cutoff=log2(exp(5)))
}

## End(Not run)

makePWMEmpiricalBackground

*Make an empirical P-value background*

**Description**

Make a background appropriate for empirical P-value calculation. The provided set of background sequences is concatenated into a single long sequence which is then scanned with the motifs and raw scores are saved. This object can be very large.

**Usage**

```r
makePWMEmpiricalBackground(
  bg.seq,
  motifs,
  bg.pseudo.count = 1,
  bg.source = "",
  verbose = TRUE,
  ...
)
```

**Arguments**

- `bg.seq` a set of background sequences, either a list of DNAString object or DNAStringSet object
- `motifs` a set of motifs, either a list of frequency matrices, or a list of PWM objects. If frequency matrices are given, the background distribution is fitted from `bg.seq`
- `bg.pseudo.count` the pseudo count which is shared between nucleotides when frequency matrices are given
- `bg.source` a free-form textual description of how the background was generated
- `verbose` if to produce verbose output
- `...` currently unused (this is for convenience for `makeBackground` function)

**Details**

For reliable P-value calculation the size of the background set needs to be at least seq.len / min.P.value.

For instance, to get P-values at a resolution of 0.001 for a single sequence of 500bp, we would need a background of at least \(500/0.001 = 500\)kb. This ensures that we can make 1000 independent 500bp samples from this background to properly estimate the P-value. For a group of sequences, we would take seq.len to be the total length of all sequences in a group.
makePWMGEVBackground

Make a GEV background distribution

Description

Construct a lognormal background distribution for a set of sequences. Sequences concatenated are binned in 'bg.len' chunks and lognormal distribution fitted to them.

Usage

makePWMGEVBackground(
  bg.seq,
  motifs,
  bg.pseudo.count = 1,
  bg.len = seq(200, 2000, 200),
  bg.source = "",
  verbose = TRUE,
  fit.log = TRUE
)

Arguments

bg.seq a set of background sequences, either a list of DNASTring object or DNASTringSet object
motifs a set of motifs, either a list of frequency matrices, or a list of PWM objects. If frequency matrices are given, the background distribution is fitted from bg.seq.
bg.pseudo.count the pseudo count which is shared between nucleotides when frequency matrices are given
bg.len the length range of background chunks
bg.source a free-form textual description of how the background was generated
verbose if to produce verbose output
fit.log if to fit log odds (instead of odds)
Examples

## Not run:
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # make background for MotifDb motifs using 2kb promoters of all D. melanogaster transcripts
  if(requireNamespace("BSgenome.Dmelanogaster.UCSC.dm3"))
    makePWMGEVBackground(Dmelanogaster$upstream2000, MotifDb.Dmel.PFM)
}
## End(Not run)

makePWMLognBackground  Make a lognormal background distribution

Description

Construct a lognormal background distribution for a set of sequences. Sequences concatenated are binned in 'bg.len' chunks and lognormal distribution fitted to them.

Usage

makePWMLognBackground(
  bg.seq,
  motifs,
  bg.pseudo.count = 1,
  bg.len = 250,
  bg.len.sizes = 2^c(0:4),
  bg.source = "",
  verbose = TRUE,
  algorithm = "default"
)

Arguments

bg.seq  a set of background sequences, either a list of DNASTring object or DNASTringSet object
motifs  a set of motifs, either a list of frequency matrices, or a list of PWM objects. If frequency matrices are given, the background distribution is fitted from bg.seq.
bg.pseudo.count  the pseudo count which is shared between nucleotides when frequency matrices are given
bg.len  background sequences will be split into tiles of this length (default: 250bp)
bg.len.sizes  background tiles will be joined into bigger tiles containing this much smaller tiles. The default is 2^c(0:4), which with bg.len translates into 250bp, 500bp, 1000bp, 1500bp, 2000bp, 4000bp. Note this is only used in the "human" algorithm.
makePWMPvalCutoffBackground

Construct a cutoff background from empirical background

Description

This function takes already calculated empirical background distribution and chooses cutoff for each motif based on P-value cutoff for individual sites.

Usage

makePWMPvalCutoffBackground(bg.p, p.value = 0.001, bg.source = "")

Arguments

- **bg.p**: an object of class PWMEmpiricalBackground
- **p.value**: the P-value used to find cutoffs for each of the motifs
- **bg.source**: textual description of background source

Value

an object of type PWMCutoffBackground

Examples

```r
## Not run:
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

# make background for MotifDb motifs using 2kb promoters of all D. melanogaster transcripts
if(requireNamespace("BSgenome.Dmelanogaster.UCSC.dm3"))
  makePWMLognBackground(Dmelanogaster$upstream2000, MotifDb.Dmel.PFM)
}

## End(Not run)
```
makePWMPvalCutoffBackgroundFromSeq

Construct a P-value cutoff background from a set of sequences

Description

This function creates a P-value cutoff background for motif enrichment.

Usage

makePWMPvalCutoffBackgroundFromSeq(
  bg.seq,
  motifs,
  p.value = 0.001,
  bg.pseudo.count = 1,
  bg.source = "",
  verbose = TRUE
)

Arguments

bg.seq a set of background sequences, either a list of DNAString object or DNAStringSet object
motifs a set of motifs, either a list of frequency matrices, or a list of PWM objects. If frequency matrices are given, the background distribution is fitted from bg.seq.
p.value the P-value used to find cutoffs for each of the motifs
bg.pseudo.count the pseudo count which is shared between nucleotides when frequency matrices are given
bg.source textual description of background source
verbose if to print verbose output

Value

an object of type PWMCutoffBackground
Examples

```r
## Not run:
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # use the empirical background to pick a threshold and make cutoff background
  makePWMPvalCutoffBackground(Dmelanogaster$upstream2000, 0.001)
}

## End(Not run)
```

### makeStartEndPos

Divide total.len into fragments of length len by providing start.end positions

```r
makeStartEndPos(total.len, len)
```

**Arguments**

- `total.len`: total available length to be subdivided
- `len`: size of the individual chunk

**Value**

a data.frame containing paired up start.end positions

### matrixShuffleZscorePerSequence

Obtain z-score for motif column shuffling

```r
matrixShuffleZscorePerSequence(scores, sequences, pwms, cutoff = NULL, B = 30)
```

**Description**

All PWMs are shuffled at the same time. This function would be too slow to produce empirical P-values, thus we return a z-score from a small number of shuffles.
Arguments

scores a set of already calculated scores
sequences either one sequence or a list/set of sequences (objects of type DNAString or DNAStringSet)
pwms a list of PWMs
cutoff if NULL, will use affinity, otherwise will use number of hits over this log2 odds cutoff
B number of replicates, i.e. PWM column shuffles

Details

The z-scores are calculated for each sequence individually.

maxAligned

Returned the aligned motif parts

Description

This function takes the offset of first motif relative to second and chops off the end of both motifs that are not aligned. It returns a list containing only the columns that align.

Usage

maxAligned(m1, m2, offset)

Arguments

m1 frequency matrix of first motif
m2 frequency matrix of second motif
offset a number of nucleotides by which the first motif is offsetted compared to the second

Value

a list of column-trimmed motifs m1, m2
motifDiffEnrichment

Differential motif enrichment

Description

Test for differential enrichment between two groups of sequences

Usage

motifDiffEnrichment(
  sequences1,
  sequences2,
  pwms,
  score = "autodetect",
  bg = "autodetect",
  cutoff = log2(exp(4)),
  verbose = TRUE,
  res1 = NULL,
  res2 = NULL
)

Arguments

sequences1 First set of sequences. Can be either a single sequence (an object of class DNAString), or a list of DNAString objects, or a DNAStringSet object.

sequences2 Second set of sequences. Can be either a single sequence (an object of class DNAString), or a list of DNAString objects, or a DNAStringSet object.

pwms this parameter can take multiple values depending on the scoring scheme and background correction used. When the method parameter is set to "autodetect", the following default algorithms are going to be used:

  • if pwms is a list containing either frequency matrices or a list of PWM objects then the "affinity" algorithm is selected. If frequency matrices are given, they are converted to PWMs using uniform background. For best performance, convert frequency matrices to PWMs before calling this function using realistic genomic background.

  • Otherwise, appropriate scoring scheme and background correction are selected based on the class of the object (see below).

score this parameter determines which scoring scheme to use. Following scheme as available:

  • "autodetect" - default value. Scoring method is determined based on the type of pwms parameter.

  • "affinity" - use threshold-free affinity scores without a background. The pwms parameter can either be a list of frequency matrices, PWM objects, or a PWMLognBackground object.
motifEcdf

Calculate the empirical distribution score distribution for a set of motifs

Description

Calculate the empirical distribution score distribution for a set of motifs.
motifEnrichment

Usage

motifEcdf(
  motifs,
  organism = NULL,
  bg.seq = NULL,
  quick = FALSE,
  pseudo.count = 1
)

Arguments

motifs a set of motifs, either a list of frequency matrices, or a list of PWM objects. If frequency matrices are given, the background distribution is fitted from bg.seq.

organism either a name of the organisms for which the background should be compiled (supported names are "dm3", "mm9" and "hg19"), or a BSgenome object (see BSgenome package).

bg.seq a set of background sequence (either this or organism needs to be specified!). Can be a DNAString or DNAStringSet object.

quick if to do the fitting only on a small subset of the data (only in combination with organism). Useful only for code testing!

pseudo.count the pseudo count which is shared between nucleotides when frequency matrices are given

Value

a list of ecdf objects (see help page for ecdf for usage).

motifEnrichment  Motif enrichment

Description

Calculate motif enrichment using one of available scoring algorithms and background corrections.

Usage

motifEnrichment(
  sequences,
  pwms,
  score = "autodetect",
  bg = "autodetect",
  cutoff = NULL,
  verbose = TRUE,
  motif.shuffles = 30,
  B = 1000,
  group.only = FALSE
)
Arguments

sequences: the sequences to be scanned for enrichment. Can be either a single sequence (an object of class DNAString), or a list of DNAString objects, or a DNAStringSet object.

pwms: this parameter can take multiple values depending on the scoring scheme and background correction used. When the method parameter is set to "autodetect", the following default algorithms are going to be used:

- if pwms is a list containing either frequency matrices or a list of PWM objects then the "affinity" algorithm is selected. If frequency matrices are given, they are converted to PWMs using uniform background. For best performance, convert frequency matrices to PWMs before calling this function using realistic genomic background.
- Otherwise, appropriate scoring scheme and background correction are selected based on the class of the object (see below).

score: this parameter determines which scoring scheme to use. Following scheme as available:

- "autodetect" - default value. Scoring method is determined based on the type of pwms parameter.
- "affinity" - use threshold-free affinity score. The pwms parameter can either be a list of frequency matrices, PWM objects, or a PWMLognBackground object.
- "cutoff" - use number of motif hits above a score cutoff. The pwms parameter can either be a list of frequency matrices, PWM objects, or a PWMCutoffBackground object.
- "clover" - use the Clover algorithm (Frith et al, 2004). The Clover score of a single sequence is identical to the affinity score, while for a group of sequences is an average of products of affinities over all sequence subsets.

bg: this parameter determines how the raw score is compared to the background distribution.

- "autodetect" - default value. Background correction is determined based on the type of the pwms parameter.
- "logn" - use a lognormal distribution background pre-computed for a set of PWMs. This requires pwms to be of class PWMLognBackground.
- "z" - use a z-score for the number of significant motif hits compared to background number of hits. This requires pwms to be of class PWMCutoffBackground.
- "pval" - use empirical P-value based on a set of background sequences. This requires pwms to be of class PWMEmpiricalBackground. Note that PWMEmpiricalBackground objects tend to be very large so that the empirical P-value can be calculated in reasonable time.
- "ms" - shuffle columns of motif matrices and use that as basis for P-value calculation. Note that since the sequences need to rescanned with all of the new shuffled motifs this can be very slow. Also, this also works only on *individual* sequences, not groups.
- "none" - no background correction

cutoff: the score cutoff for a significant motif hit if scoring scheme "cutoff" is selected.
verbose if to print verbose output

motif.shuffles number of times to shuffle motifs if using "ms" background correction

B number of replicates when calculating empirical P-value

group.only if to return statistics only for the group of sequences, not individual sequences. In the case of empirical background the P-values for individual sequences are not calculated (thus saving time), for other backgrounds they are calculated but not returned.

Details

This function provides an interface to all algorithms available in PWMEnrich to find motif enrichment in a single or a group of sequences with/without background correction.

Since for all algorithms the first step involves calculating raw scores without background correction, the output always contains the scores without background correction together with (optional) background-corrected scores.

Unless otherwise specified the scores are returned both separately for each sequence (without/with background) and for the whole group of sequences (without/with background).

To use a background correction you need to supply a set of PWMs with precompiled background distribution parameters (see function makeBackground). When such an object is supplied as the pwm parameter, the scoring scheme and background correction are automatically determined.

There are additional packages with already pre-computed background (e.g. see package PWMEnrich.Dmelanogaster.background). Please refer to (Stojnic & Adryan, 2012) for more details on the algorithms.

Value

a MotifEnrichmentResults object containing a subset following elements:

- "score" - scoring scheme used
- "bg" - background correction used
- "params" - any additional parameters
- "sequences" - the set of sequences used
- "pwms" - the set of pwms used
- "sequence.nobg" - per-sequence scores without any background correction. For "affinity" and "clover" a matrix of mean affinity scores; for "cutoff" number of significant hits above a cutoff
- "sequence.bg" - per-sequence scores after background correction. For "logn" and "pval" the P-value (smaller is better); for "z" and "ms" background corrections the z-scores (bigger is better).
- "group.nobg" - aggregate scores for the whole group of sequences without background correction. For "affinity" and "clover" the mean affinity over all sequences in the set; for "cutoff" the total number of hits in all sequences.
- "group.bg" - aggregate scores for the whole group of sequences with background correction. For "logn" and "pval", the P-value for the whole group (smaller is better); for "z" and "ms" the z-score for the whole set (bigger is better).
motifEnrichment

- "sequence.norm" - (only for "logn") the length-normalized scores for each of the sequences. Currently only implemented for "logn", where it returns the values normalized from LogN(0,1) distribution
- "group.norm" - (only for "logn") similar to sequence.norm, but for the whole group of sequences

References


Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){

###
# load the pre-compiled lognormal background

# scan two sequences for motif enrichment
sequences = list(DNAString("GAAGTATCAAGTGACCAGTAGATTGAAGTAGACCAGTC"),
                 DNAString("AGGTAGATAGAACAGTAGGCAATGGGGGAAATTGAGAGTC"))
res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)

# most enriched in both sequences (lognormal background P-value)
head(motifRankingForGroup(res))

# most enriched in both sequences (raw affinity, no background)
head(motifRankingForGroup(res, bg=FALSE))

# most enriched in the first sequence (lognormal background P-value)
head(motifRankingForSequence(res, 1))

# most enriched in the first sequence (raw affinity, no background)
head(motifRankingForSequence(res, 1, bg=FALSE))

###
# Load the pre-compiled background for hit-based motif counts with cutoff of P-value = 0.001
data(PWMPvalueCutoff1e3.dm3.MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")

res.count = motifEnrichment(sequences, PWMPvalueCutoff1e3.dm3.MotifDb.Dmel)

# Enrichment in the whole group, z-score for the number of motif hits
head(motifRankingForGroup(res))

# First sequence, sorted by number of motif hits with P-value < 0.001
head(motifRankingForSequence(res, 1, bg=FALSE))

}
```
MotifEnrichmentReport-class

A report class with formatted results of motif enrichment

Description

The columns stored in this object will depend on the type of the report (either for group of sequences, or individual sequences).

Slots

d: a DataFrame object that contains the main tabular report data

MotifEnrichmentResults-class

A wrapper class for results of motifEnrichment() that should make it easier to access the results.

Description

Note that this is only a wrapper around a list which is the return value in PWMEnrich 1.3 and as such it provides the same interface as a list (for backward compatibility), with some additional methods.

Slots

res: a list of old results with elements such as: sequence.bg, sequence.nobg, group.bg, group.nobg

motifIC

Information content for a PWM or PFM

Description

Information content for a PWM or PFM

Usage

```r
motifIC(
motif,
prior.params = c(A = 0.25, C = 0.25, G = 0.25, T = 0.25),
bycol = FALSE
)
```
motifPrAUC

**Arguments**

- **motif**  a matrix of frequencies, or a PWM object
- **prior.params**  the prior parameters to use when a matrix is given (ignored if motif is already a PWM)
- **bycol**  if to return values separately for each column

**Value**

information content in bits (i.e. log2)

**Examples**

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # the nucleotide distribution is taken from the PWM (in this case genomic background)
  motifIC(MotifDb.Dmel["ttk"])
  # information content with default uniform background because the input is a matrix,
  # not PWM object
  motifIC(MotifDb.Dmel.PFM["ttk"])
}
```

---

**motifPrAUC**  
*Calculate PR-AUC for motifs ranked according to some scoring scheme*

**Description**

Note that this function assumes that smaller values are better!

**Usage**

```r
motifPrAUC(seq.res)
```

**Arguments**

- **seq.res**  a matrix where each column represents a PWM and each row a result for a different sequence.
motifRankingForGroup,MotifEnrichmentResults-method

Get a ranking of motifs by their enrichment in the whole set of sequences

Description

Get a ranking of motifs by their enrichment in the whole set of sequences

Usage

## S4 method for signature 'MotifEnrichmentResults'
motifRankingForGroup(
  obj,
  bg = TRUE,
  id = FALSE,
  order = FALSE,
  rank = FALSE,
  unique = FALSE,
  ...
)

Arguments

obj a MotifEnrichmentResults object
bg if to use background corrected P-values to do the ranking (if available)
id if to show PWM IDs instead of target TF names
order if to output the ordering of PWMs instead of actual P-values or raw values
rank if the output should be rank of a PWM instead of actual P-values or raw values
unique if TRUE, only the best rank is taken for each TF (only when id = FALSE, order = FALSE)
... currently unused

Value

a vector of P-values or raw enrichments sorted such that the first motif is most enriched

Examples

if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # load the pre-compiled lognormal background

  # scan two sequences for motif enrichment
  sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                   DNAString("GAGGTATCAAGTGACCAGTAAGTCCCAGATGA")),
motifRankingForSequence(MotifEnrichmentResults-method)

Get a ranking of motifs by their enrichment in one specific sequence

Description

Get a ranking of motifs by their enrichment in one specific sequence

Usage

```r
## S4 method for signature 'MotifEnrichmentResults'
motifRankingForSequence(
  obj, seq.id, bg = TRUE, id = FALSE, order = FALSE, rank = FALSE, unique = FALSE,
  ...
)
```

Arguments

- `obj`: a MotifEnrichmentResults object
- `seq.id`: either the sequence number or sequence name
- `bg`: if to use background corrected P-values to do the ranking (if available)
- `id`: if to show PWM IDs instead of target TF names
motifRecoveryAUC

Calculate Recovery-AUC for motifs ranked according to some scoring scheme

Description

Note that this function assumes that smaller values are better!

Usage

motifRecoveryAUC(seq.res)
motifScores

Arguments

seq.res a matrix where each column represents a PWM and each row a result for a different sequence.

motifScores Motif affinity or number of hits over a threshold

Description

Scan a number of sequences either to find overall affinity, or a number of hits over a score threshold.

Usage

motifScores(
  sequences,
  motifs,
  raw.scores = FALSE,
  verbose = TRUE,
  cutoff = NULL
)

Arguments

sequences a set of sequences to be scanned, a list of DNAString or other scannable objects
motifs a list of motifs either as frequency matrices (PFM) or as PWM objects. If PFMs are specified they are converted to PWMs using uniform background.
raw.scores if to return raw scores (odds) for each position in the sequence. Note that scores for forward and reverse strand are concatenated into a single long vector of scores (twice the length of the sequence)
verbose if to print verbose output
cutoff if not NULL, will count number of matches with score above value specified (instead of returning the average affinity). Can either be one value, or a vector of values for each of the motifs.

Value

if raw.scores=FALSE, returns a matrix of mean scores (after cutoff if any), where columns are motifs. The returned values are either mean odd scores (not log-odd), or number of hits above a threshold; otherwise if raw.scores=TRUE, returns a list of raw score values (before cutoff)
motifScoresBigMemory

Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")

  # affinity scores
  affinity = motifScores(DNAString("CGTAGGATAAAGTAACCTAGTTGATGAAAG"), MotifDb.Dmel)

  # motif hit count with Patser score of 4
  counts = motifScores(DNAString("CGTAGGATAAAGTAACCTAGTTGATGAAAG"), MotifDb.Dmel,
                      cutoff=log2(exp(4)))

  print(affinity)
  print(counts)

  # scanning multiple sequences
  sequences = list(DNAString("CGTAGGATAAAGTAACCTAGTTGATGAAAG"),
                   DNAString("TGAGACGAAGGGGATGAGATGCGGAAGAGTGAAA"))
  affinity2 = motifScores(sequences, MotifDb.Dmel)
  print(affinity2)
}
```

motifScoresBigMemory  This is a memory intensive version of motifScore() which is about 2 times faster

Description

The parameters and functionality are the same as `motifScores`. Please refer to documentation of this function for detailed explanation of functionality.

Usage

```r
motifScoresBigMemory(
  sequences, 
  motifs, 
  raw.scores = FALSE, 
  verbose = TRUE, 
  cutoff = NULL, 
  seq.all = NULL
)
```

Arguments

<table>
<thead>
<tr>
<th>Argument</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><code>sequences</code></td>
<td>set of input sequences</td>
</tr>
<tr>
<td><code>motifs</code></td>
<td>set of input PWMs or PFM s</td>
</tr>
<tr>
<td><code>raw.scores</code></td>
<td>if to return scores for each base-pair</td>
</tr>
<tr>
<td><code>verbose</code></td>
<td>if to produce verbose output</td>
</tr>
</tbody>
</table>
motifSimilarity

Cutoff

The cutoff for calling binding sites (in base 2 log).

seq.all

Already concatenated sequences if already available (used to internally speed up things).

Details

This function is not meant to be called directly, but is indirectly called by motifScores() once a global parameters useBigMemory is set.

See Also

motifScores

Description

This function calculates the normalized motif correlation as a measure of motif frequency matrix similarity.

Usage

motifSimilarity(m1, m2, trim = 0.4, self.sim = FALSE)

Arguments

m1

Matrix with four rows representing the frequency matrix of first motif

m2

Matrix with four rows representing the frequency matrix of second motif

trim

Bases with information content smaller than this value will be trimmed off both motif ends

self.sim

If to calculate self similarity (i.e. without including offset=0 in alignment)

Details

This score is essentially a normalized version of the sum of column correlations as proposed by Pietrokovski (1996). The sum is normalized by the average motif length of m1 and m2, i.e. \((\text{ncol}(m1) + \text{ncol}(m2))/2\). Thus, for two identical motifs this score is going to be 1. For unrelated motifs the score is going to be typically around 0.

Motifs need to aligned for this score to be calculated. The current implementation tries all possible ungapped alignment with a minimal of two basepair matching, and the maximal score over all alignments is returned.

Motif 1 is aligned both to Motif 2 and its reverse complement. Thus, the motif similarities are the same if the reverse complement of any of the two motifs is given.
**References**


**Examples**

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # calculate the similarity of tin and vnd motifs (which are almost identical)
  motifSimilarity(MotifDb.Dmel.PFM[['tin']], MotifDb.Dmel.PFM[['vnd']])

  # similarity of two unrelated motifs
  motifSimilarity(MotifDb.Dmel.PFM[['tin']], MotifDb.Dmel.PFM[['ttk']])
}
```

---

**Names of variables**

Columns stored in the motif enrichment report

**Usage**

```r
## S4 method for signature 'MotifEnrichmentReport'
names(x)

## S4 method for signature 'MotifEnrichmentReport'
x$name

## S4 method for signature 'MotifEnrichmentReport'
x[i, j, ..., drop = TRUE]
```

**Arguments**

- `x` the MotifEnrichmentReport object
- `name` the variable name
- `i` the row selector
- `j` unused
- `...` unused
- `drop` unused (always FALSE)

**Value**

the names of the variables
names,MotifEnrichmentResults

*Names of variables*

**Description**

Name of different pieces of information associated with MotifEnrichmentResults.

**Usage**

```r
## S4 method for signature 'MotifEnrichmentResults'
names(x)
```

```r
## S4 method for signature 'MotifEnrichmentResults'
x$name
```

**Arguments**

- **x**
  - the MotifEnrichmentResults object

- **name**
  - the variable name

**Value**

the names of the variables

---

names,PWM

*Names of variables*

**Description**

Name of different pieces of information associated with PWM.

Returns the motif length, i.e. the number of columns in the PWM.

**Usage**

```r
## S4 method for signature 'PWM'
names(x)
```

```r
## S4 method for signature 'PWM'
x$name
```

```r
## S4 method for signature 'PWM'
length(x)
```
Arguments

x the PWM object
name the variable name

Value

the names of the variables

names,PWMCutoffBackground

Names of variables

Description

Name of different pieces of information associated with PWMCutoffBackground

Usage

```r
## S4 method for signature 'PWMCutoffBackground'
names(x)

## S4 method for signature 'PWMCutoffBackground'
x$name
```

Arguments

x the PWMCutoffBackground object
name the variable name

Value

the names of the variables

names,PWMEmpiricalBackground

Names of variables

Description

Name of different pieces of information associated with PWMEmpiricalBackground
Usage

### S4 method for signature 'PWMEmpiricalBackground'

`names(x)`

### S4 method for signature 'PWMGEVBackground'

`x$name`

Arguments

- **x**: the PWMEmpiricalBackground object
- **name**: the variable name

Value

the names of the variables

---

**names,PWMGEVBackground**

*Names of variables*

Description

Name of different pieces of information associated with PWMGEVBackground

Usage

### S4 method for signature 'PWMGEVBackground'

`names(x)`

### S4 method for signature 'PWMGEVBackground'

`x$name`

Arguments

- **x**: the PWMGEVBackground object
- **name**: the variable name

Value

the names of the variables
Description

Name of different pieces of information associated with PWMLognBackground

Usage

```
## S4 method for signature 'PWMLognBackground'
names(x)

## S4 method for signature 'PWMLognBackground'
x$name
```

Arguments

- `x`: the PWMLognBackground object
- `name`: the variable name

Value

the names of the variables

---

**PFMtoPWM**

*Convert frequencies into motifs using PWMUnscaled*

Description

Note that this function is deprecated and replaced by toPWM().

Usage

```
PFMtoPWM(
  motifs,
  id = names(motifs),
  name = names(motifs),
  seq.count = NULL,
  ...
)
```
plot.MotifEnrichmentReport,missing-method

Arguments

- **motifs**: a list of motifs represented as matrices of frequencies (PFM)
- **id**: the set of IDs for the motifs (defaults to names of the 'motifs' list)
- **name**: the set of names for the motifs (defaults to names of the 'motifs' list)
- **seq.count**: if frequencies in the motifs are normalized to 1, provides a vector of sequence counts (e.g. for MotifDb motifs)
- **...**: other parameters to PWMMUnscaled

Examples

```r
## Not run:
if (requireNamespace("PWMEnrich.Dmelanogaster.background")) {
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  # convert to PWM with uniform background
  PFMtoPWM(MotifDb.Dmel.PFM)

  # get background for drosophila (quick mode on a reduced dataset)
  prior = getBackgroundFrequencies("dm3", quick=TRUE)

  # convert with genomic background
  PFMtoPWM(MotifDb.Dmel.PFM, prior.params=prior)
}
## End(Not run)
```

plot.MotifEnrichmentReport,missing-method

*Plot the motif enrichment report*

Description

Plots a graphical version of the motif enrichment report. Note that all values are plotted, if you want to plot only a subset of a report, first select this subset (see examples).

Usage

```r
## S4 method for signature 'MotifEnrichmentReport,missing'
plot(
  x,
  y,
  fontsize = 14,
  id.fontsize = fontsize,
  header.fontsize = fontsize,
  widths = NULL,
  ...)
```
Arguments

- **x**: a MotifEnrichmentReport object
- **y**: unused
- **fontsize**: font size to use in the plot
- **id.fontsize**: font size to use for the motif IDs
- **header.fontsize**: font size of the header
- **widths**: the relative widths of columns
- **...**: unused

```r
### load the pre-compiled lognormal background data
load(data(PWMLogn.dm3.MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")
# scan two sequences for motif enrichment
sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                 DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))
res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)
# produce a report for all sequences taken together
r = groupReport(res)
# plot the top 10 most enriched motifs
plot(r[1:10])
```

Description

This function produces a sequence logo (via package seqLogo).

Usage

```r
## S4 method for signature 'PWM,missing'
plot(x, y, ...)
```

Arguments

- **x**: the PWM object
- **y**: unused
- **...**: other parameters to pass to seqLogo’s plot function

Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")
  # plot the tinman motif from MotifDb
  plot(MotifDb.Dmel["tin"])}
```
plotMotifScores

Plot the raw motifs scores as returned by motifScores()

Description

This function visualises the motif scores for one or more sequences. Sequences are drawn as lines, and scores are plotted as triangles at both sides of the line (corresponding to the two strands). The width of the base of the triangle corresponds to motif width and the height to the motif $\log(\text{score})$ that is positive and greater than the cutoff parameter (if specified). All scores have the same y-axis, so the heights of bars are comparable between sequences and motifs.

Usage

plotMotifScores(
  scores,
  sel.motifs = NULL,
  seq.names = NULL,
  cols = NULL,
  cutoff = NULL,
  log.fun = log2,
  main = "",
  legend.space = 0.3,
  max.score = NULL,
  trans = 0.5,
  text.cex = 0.9,
  legend.cex = 0.9,
  motif.names = NULL,
  seq.len.spacing = 8,
  shape = "rectangle"
)

Arguments

scores the list of motifs scores. Each element of the list is a matrix of scores for one sequences. The columns in the matrix correspond to different motifs. Each column contains the odds (not log-odds!) scores over both strands. For example, for a sequence of length 5, scores for a 3 bp motifs could be: c(0.1, 1, 4, NA, NA, 1, 0.3, 2, NA, NA). The first 3 numbers are odds scores starting at first three bases, and the second lot of 3 numbers is the scores starting at the same positions but with the reverse complement of the motif. The last two values are NA on both strands because we do not support partial motif hits.

sel.motifs a vector of motif names. Use this parameter to show the motif hits to only a subset of motifs for which the scores are available.

seq.names a vector of sequence names to show in the graph. If none specified, the sequences will be named Sequence 1, Sequence 2, ...
**plotMotifScores**

- **cols**: a vector of colours to use to colour code motif hits. If none are specified, the current palette will be used.

- **cutoff**: either a single value, or a vector of values. The values are PWM cutoffs after `log.fun` (see below). Only motif scores above these cutoffs will be shown. If a single values is specified, it will be used for all PWMs, otherwise the vector needs to specify one cutoff per PWM.

- **log.fun**: the logarithm function to use to calculate log-odds. By default `log2` is used for consistency with Biostrings.

- **main**: the main title

- **legend.space**: the proportion of horizontal space to reserve for the legend. The default is 30%.

- **max.score**: the maximal log-odds score used to scale all other scores. By default this values is automatically determined, but it can also be set manually to make multiple plots comparable.

- **trans**: the level of transparency. By default 50% transparency to be able to see overlapping binding sites

- **text.cex**: the scaling factor for sequence names

- **legend.cex**: the scaling factor for the legend

- **motif.names**: optional vector of motif names to show instead of those present as column names in scores

- **seq.len.spacing**: the spacing (in bp units) between the end of the sequence line and the text showing the length in bp

- **shape**: the shape to use to draw motif occurrences, valid values are "rectangle" (default), "line" and "triangle"

**Examples**

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # Load Drosophila PWMs
  data(MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")

  # two sequences of interest
  sequences = list(DNAString("GAAGTATCAAGTGACCAGGTGAAGTCCCAGATGA"),
                   DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))

  # select the tinman and snail motifs
  pwms = MotifDb.Dmel[c("tin", "sna")]

  # get the raw score that will be plotted
  scores = motifScores(sequences, pwms, raw.scores=TRUE)

  # plot the scores in both sequences, green for tin and blue for sna
  plotMotifScores(scores, cols=c("green", "blue"))
}
```
plotMultipleMotifs  

Plot multiple motifs in a single plot

Description

Individual motif logos are plotted on a rows x cols grid. This function is a convenience interface for the seqLogoGrid function that deals with viewpoint placement in a matrix-like grid layout.

Usage

```
plotMultipleMotifs(pwms,
    titles = names(pwms),
    rows = ceiling(sqrt(length(pwms))),
    cols = ceiling(sqrt(length(pwms))),
    xmargin.scale = 0.4,
    ymargin.scale = 0.4,
    ...
)
```

Arguments

- `pwms`  
a list of PWM objects or frequency matrices
- `titles`  
a character vector of titles for each of the plots
- `rows`  
number of rows in the grid
- `cols`  
number or cols in the grid
- `xmargin.scale`  
the scaling parameter for the X-axis margin. Useful when plotting more than one logo on a page
- `ymargin.scale`  
the scaling parameter for the Y-axis margin. Useful when plotting more than one logo on a page
- `...`  
other parameters passed to seqLogoGrid()

Details

By default will try to make a square grid plot that would fit all the motifs and use list names as captions.
plotPFM  

Plot a PFM (not PWM) using seqLogo

Description

Plot a PFM (not PWM) using seqLogo

Usage

plotPFM(pfm, ...)

Arguments

pfm  
a matrix where rows are the four nucleotides

...  
additional parameters for plot()

plotTopMotifsGroup,MotifEnrichmentResults-method  
Plot the top N enrichment motifs in a group of sequences

Description

Plot the top N enrichment motifs in a group of sequences

Usage

## S4 method for signature 'MotifEnrichmentResults'
plotTopMotifsGroup(obj, n, bg = TRUE, id = FALSE, ...)

Arguments

obj  
a MotifEnrichmentResults object

n  
the number of top ranked motifs to plot

bg  
if to use background corrected P-values to do the ranking (if available)

id  
if to show PWM IDs instead of target TF names

...  
other parameters passed to plotMultipleMotifs()
Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # load the pre-compiled lognormal background

  # scan two sequences for motif enrichment
  sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                   DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))
  res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)

  # plot the top 4 motifs in a 2x2 grid
  plotTopMotifsGroup(res, 4)

  # plot top 3 motifs in a single row
  plotTopMotifsGroup(res, 3, row=1, cols=3)
}
```

Description

Plot the top N enrichment motifs in a single sequence

Usage

```r
## S4 method for signature 'MotifEnrichmentResults'
plotTopMotifsSequence(obj, seq.id, n, bg = TRUE, id = FALSE, ...)
```

Arguments

- `obj`: a MotifEnrichmentResults object
- `seq.id`: either the sequence number or sequence name
- `n`: the number of top ranked motifs to plot
- `bg`: if to use background corrected P-values to do the ranking (if available)
- `id`: if to show PWM IDs instead of target TF names
- `...`: other parameters passed to `plotMultipleMotifs()`
Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # load the pre-compiled lognormal background

  # scan two sequences for motif enrichment
  sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                   DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))

  res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)

  # plot the top 4 motifs in a 2x2 grid
  plotTopMotifsSequence(res, 1, 4)

  # plot top 3 motifs in a single row
  plotTopMotifsSequence(res, 1, 3, row=1, cols=3)
}
```

---

**PWM-class**

A class that represents a Position Weight Matrix (PWM)

**Description**

A class that represents a Position Weight Matrix (PWM)

**Slots**

- **id**: a systematic ID given to this PWM, could include the source, version, etc
- **name**: the name of the transcription factor (TF) to which the PWM corresponds to
- **pfm**: Position Frequency Matrix (PFM) from which the PWM is derived
- **prior.params**: Defines prior frequencies of the four bases (A,C,G,T), a named vector. These will be added to individual values for the PFM and at the same time used as background probabilities
- **pwm**: Final Position Weight Matrix (PWM) constructed using prior.params with logarithm base 2

---

**PWMCutoffBackground-class**

Hit count background distribution for a set of PWMs

**Description**

Hit count background distribution for a set of PWMs
Slots

bg.source: textual description of where the background distribution is derived from
bg.cutoff: the cutoff score used to find significant motif hits (in log2 odds), either a single value or a vector of values
bg.P: the density of significant motif hits per nucleotide in background
pwms: the pwms for which the background has been compiled

PWMEmpiricalBackground-class

Background for calculating empirical P-values

Description

This object contains raw scores for one very long sequence, thus it can be very large.

Slots

bg.source: textual description of where the background distribution is derived from
bg.fwd: affinity scores (odds) for the forward strand. PWMS as columns
bg.rev: affinity scores (odds) for the reverse strand. PWMS as columns
pwms: the pwms for which the background has been compiled

PWMGEVBackground-class

Generalized Extreme Values (GEV) background for P-values

Description

The three parameters of the GEV distribution are fitted by doing linear regression on log of sequence length.

Slots

bg.source: textual description of where the background distribution is derived from
bg.loc: linear regression model for estimating the location parameter based on log(L), list of lm objects of PWMS
bg.scale: linear regression model for estimating the scale parameter based on log(L), list of lm objects of PWMS
bg.shape: linear regression model for estimating the shape parameter based on log(L), list of lm objects of PWMS
pwms: the pwms for which the background has been compiled
**PWMLognBackground-class**

*Lognormal background distribution for a set of PWMs*

**Description**

Lognormal background distribution for a set of PWMs

**Slots**

- **bg.source**: textual description of where the background distribution is derived from
- **bg.len**: the length to which the background is normalized to. This is a vector of values, can have a different value for each motif.
- **bg.mean**: the mean value of the lognormal distribution at bg.len
- **bg.sd**: the standard deviation of the lognormal distribution at bg.len
- **pwms**: the pwms for which the background has been compiled

---

**PWMUnscaled**

*Create a PWM from PFM*

**Description**

The PWM function from Biostrings without unit scaling

**Usage**

```r
PWMUnscaled(
  x, 
  id = "", 
  name = "", 
  type = c("log2probratio", "prob"), 
  prior.params = c(A = 0.25, C = 0.25, G = 0.25, T = 0.25), 
  pseudo.count = prior.params, 
  unit.scale = FALSE, 
  seq.count = NULL 
)
```

**Arguments**

- **x**: the integer count matrix representing the motif, rows as nucleotides
- **id**: a systematic ID given to this PWM, could include the source, version, etc
- **name**: the name of the transcription factor (TF) to which the PWM corresponds to
type
prior.params
pseudo.count
unit.scale
seq.count

the type of PWM calculation, either as log2-odds, or posterior probability (frequency matrix)
the pseudocounts for each of the nucleotides
the pseudo-count values if different from priors
if to unit.scale the pwm (default is no unit scaling)
if x is a normalised PFM (i.e. with probabilities instead of sequence counts), then this sequence count will be used to convert x into a count matrix

Details
By default the Biostrings package scales the log-odds score so it is within 0 and 1. In this function we take a more traditional approach with no unit scaling and offer unit scaling as an additional parameter.
See ?PWM from Biostrings for more information on input arguments.

Value
a new PWM object representing the PWM

Examples
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  ttk = MotifDb.Dmel.PFM[["ttk"]]

  # make a PWM with uniform background
  PWMUnscaled(ttk, id="ttk-JASPAR", name="ttk")

  # custom background
  PWMUnscaled(ttk, id="ttk-JASPAR", name="ttk",
              prior.params=c("A" = 0.2, "C" = 0.3, "G" = 0.3, "T" = 0.2))

  # get background for drosophila (quick mode on a reduced dataset)
  prior = getBackgroundFrequencies("dm3", quick=TRUE)

  # convert using genomic background
  PWMUnscaled(ttk, id="ttk-JASPAR", name="ttk", prior.params=prior)
}

rankingProcessAndReturn
A helper function for motifRankingForGroup and motifRankingForSequence with the common code
**readJASPAR**

**Description**

A helper function for motifRankingForGroup and motifRankingForSequence with the common code

**Usage**

`rankingProcessAndReturn(res, r, id, order, rank, unique, decreasing)`

**Arguments**

- `res` the list of results from MotifEnrichmentResults object
- `r` the vector of raw results that needs to be processed
- `id` if to return IDs instead of names
- `order` if to return the ordering of motifs
- `rank` if to return the rank of motifs
- `unique` if to remove duplicates
- `decreasing` specifies the sorting order

**readJASPAR**

Read motifs in JASPAR format

**Description**

Read motifs in JASPAR format

**Usage**

`readJASPAR(file, remove.ids = FALSE)`

**Arguments**

- `file` the filename
- `remove.ids` if to strip JASPAR ID’s from motif names, e.g. "MA0211.1 bap" would become just "bap"

**Value**

a list of matrices representing motifs (with four nucleotides as rows)
readMotifs  Read in motifs in JASPAR or TRANSFAC format

Description

The format is autodetected based on file format. If the autodetection fail then the file cannot be read.

Usage

readMotifs(file, remove.acc = FALSE)

Arguments

file

the filename

remove.acc

if to remove accession numbers. If TRUE, the AC entry in TRANSFAC files is ignored, and the accession is stripped from JASPAR, e.g. motif with name "MA0211.1 bap" would become just "bap". If FALSE, both the AC and ID are used to generate the TRANSFAC name and the original motif names are preserved in JASPAR files.

Value

a list of 4xL matrices representing motifs (four nucleotides as rows)

Examples

# read in example TRANSFAC motifs without accession codes (just IDs)
readMotifs(system.file(package = "PWMEnrich", dir = "extdata", file = "example.transfac"),
remove.acc = TRUE)

# read in the JASPAR insects motifs provided as example
readMotifs(system.file(package = "PWMEnrich", dir = "extdata", file = "jaspar-insecta.jaspar"),
remove.acc = TRUE)

readTRANSFAC  Read in motifs in TRANSFAC format

Description

Read in motifs in TRANSFAC format

Usage

readTRANSFAC(file, remove.acc = TRUE)
registerCoresPWMEnrich

Description

Certain functions (like motif scanning) can be parallelized in PWMEnrich. This function registers a number of parallel cores (via core package parallel) to be used in code that can be parallelized. After this function is called, all further PWMEnrich function calls will run in parallel if possible.

Arguments

file the filename
remove.acc if to ignore transfac accession numbers

Value

The value is a list of matrices representing motifs (with four nucleotides as rows).

registerCoresPWMEnrich

Register than PWMEnrich can use parallel CPU cores

Usage

registerCoresPWMEnrich(numCores = NA)

Arguments

numCores number of cores to use (default to take all cores), or NULL if no parallel execution is to be used

Details

By default parallel execution is turned off. To turn it off after using it, call this function by passing NULL.

Examples

## Not run:
registerCoresPWMEnrich(4) # use 4 CPU cores in PWMEnrich
registerCoresPWMEnrich() # use maximal number of CPUs
registerCoresPWMEnrich(NULL) # do not use parallel execution

## End(Not run)
reverseComplement, PWM-method

Reverse complement for the PWM object

Description

Finds the reverse complement of the PWM

Usage

## S4 method for signature 'PWM'
reverseComplement(x, ...)

Arguments

x  an object of type PWM
... unused

Value

an object of type PWM that is reverse complement of x

Examples

if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel.PFM, package = "PWMEnrich.Dmelanogaster.background")

  reverseComplement(MotifDb.Dmel.PFM[["ttk"]]) # reverse complement of the ttk PWM
}

scanWithPWM

Scan the whole sequence on both strands

Description

The whole sequence is scanned with a PWM and scores returned beginning at each position. Partial motif matches are not done, thus the last #[length of motif]-1 scores are NA.
scanWithPWM

Usage

scanWithPWM(
  pwm,  # PWM object
  dna,  # a DNAString or other sequence from Biostrings
  pwm.rev = NULL,  # the reverse complement for a pwm (if it is already pre-computed)
  odds.score = FALSE,  # if to return raw scores in odds (not logodds) space
  both.strands = FALSE,  # if to return results on both strands
  strand.fun = "mean"  # which function to use to summarise values over two strands (default is "mean")
)

Arguments

- **pwm**: PWM object
- **dna**: a DNAString or other sequence from Biostrings
- **pwm.rev**: the reverse complement for a pwm (if it is already pre-computed)
- **odds.score**: if to return raw scores in odds (not logodds) space
- **both.strands**: if to return results on both strands
- **strand.fun**: which function to use to summarise values over two strands (default is "mean")

Details

The function returns either an odds average (*not* log-odds average), maximal score on each strand, or scores on both strands.

The function by default returns the score in log2 following the package Biostrings.

Value

a vector representing scores starting at each position, or a matrix with score in the two strands

Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  data(MotifDb.Dmel, package = "PWMEnrich.Dmelanogaster.background")
  ttk = MotifDb.Dmel["ttk"]

  # odds average over the two strands expressed as log2-odds
  scanWithPWM(ttk, DNAString("CGTAGGATAAAGTAACCT"))

  # log2-odds scores on both strands
  scanWithPWM(ttk, DNAString("CGTAGGATAAAGTAACCT"), both.strands=TRUE)
}
```
seqLogoGrid

Draw a motif logo on an existing viewport

Description

This function comes from the seqLogo package. It has been modified to remove some unnecessary code as suggested by W Huber (https://stat.ethz.ch/pipermail/bioconductor/2010-September/035267.html).

Usage

seqLogoGrid(
pwm,
ic.scale = TRUE,
xaxis = TRUE,
yaxis = TRUE,
xfontsize = 10,
yfontsize = 10,
xmargin.scale = 1,
ymargin.scale = 1,
title = "",
titlefontsize = 15
)

Arguments

- **pwm**: numeric The 4xW position weight matrix.
- **ic.scale**: logical If TRUE, the height of each column is proportional to its information content. Otherwise, all columns have the same height.
- **xaxis**: logical If TRUE, an X-axis will be plotted.
- **yaxis**: logical If TRUE, a Y-axis will be plotted.
- **xfontsize**: numeric Font size to be used for the X-axis.
- **yfontsize**: numeric Font size to be used for the Y-axis.
- **xmargin.scale**: the scaling parameter for the X-axis margin. Useful when plotting more than one logo on a page
- **ymargin.scale**: the scaling parameter for the Y-axis margin. Useful when plotting more than one logo on a page
- **title**: to be shown on the top
- **titlefontsize**: the fontsize of the title

Details

Use this function for more advanced plotting where the viewports are directly set up and maintained (see package grid).
Generate a motif enrichment report for a single sequence

### S4 method for signature 'MotifEnrichmentResults'

```r
sequenceReport(obj, seq.id, bg = TRUE, ...)
```

#### Arguments

- `obj`: a MotifEnrichmentResults object
- `seq.id`: the sequence index or name
- `bg`: if to use background corrected P-values to do the ranking (if available)
- `...`: unused

#### Value

A MotifEnrichmentReport object containing a table with the following columns:

- 'rank' - The rank of the PWM's enrichment in the sequence
- 'target' - The name of the PWM's target gene, transcript or protein complex.
- 'id' - The unique identifier of the PWM (if set during PWM creation).
- 'raw.score' - The raw score before P-value calculation
- 'p.value' - The P-value of motif enrichment (if available)

#### Examples

```r
if(requireNamespace("PWMEnrich.Dmelanogaster.background")){
  ###
  # load the pre-compiled lognormal background

  # scan two sequences for motif enrichment
  sequences = list(DNAString("GAAGTATCAAGTGACCAGTAAGTCCCAGATGA"),
                   DNAString("AGGTAGATAGAACAGTAGGCAATGAAGCCGATG"))
  res = motifEnrichment(sequences, PWMLogn.dm3.MotifDb.Dmel)

  # reports for the two sequences
  r1 = sequenceReport(res, 1)
  r2 = sequenceReport(res, 2)
}
```
# view the results
r1
r2

# plot the top 10 most enriched motifs in the first, and then second sequence
plot(r1[1:10])
plot(r2[1:10])

show,MotifEnrichmentReport-method

Description
show method for MotifEnrichmentReport

Usage
## S4 method for signature 'MotifEnrichmentReport'
show(object)

Arguments
object the MotifEnrichmentReport object

show,MotifEnrichmentResults-method

Description
show method for MotifEnrichmentResults

Usage
## S4 method for signature 'MotifEnrichmentResults'
show(object)

Arguments
object the MotifEnrichmentResults object
Description

show method for PWM

Usage

## S4 method for signature 'PWM'
show(object)

Arguments

object the PWM object

Description

show method for PWMCutoffBackground

Usage

## S4 method for signature 'PWMCutoffBackground'
show(object)

Arguments

object the PWMCutoffBackground object
Description

show method for PWMEmpiricalBackground

Usage

## S4 method for signature 'PWMEmpiricalBackground'
show(object)

Arguments

object the PWMEmpiricalBackground object

Description

show method for PWMGEVBackground

Usage

## S4 method for signature 'PWMGEVBackground'
show(object)

Arguments

object the PWMGEVBackground object
show.PWMLognBackground-method

Description

show method for PWMLognBackground

Usage

## S4 method for signature 'PWMLognBackground'
show(object)

Arguments

object                  the PWMLognBackground object

---

toPWM

Convert motifs into PWMs

Description

Convert motifs into PWMs

Usage

toPWM(
  motifs,
  ids = names(motifs),
  targets = names(motifs),
  seq.count = 50,
  prior = c(A = 0.25, C = 0.25, G = 0.25, T = 0.25),
  ...
)

Arguments

motifs                a list of motifs either as position probability matrices (PPM) or frequency matrices (PFMs)
ids                   the set of IDs for the motifs (defaults to names of the 'motifs' list)
targets               the set of target TF names for the motifs (defaults to names of the 'motifs' list)
seq.count             provides a vector of sequence counts for probability matrices (PPMs). Default is 50.
prior                 frequencies of the four letters in the genome. Default is uniform background.
...                    other parameters to PWMUnscaled
tryAllMotifAlignments

Try all motif alignments and return max score

Description

This function tries all offsets of motif1 compared to motif2 and returns the maximal (unnormalized) correlation score.

Usage

tryAllMotifAlignments(m1, m2, min.align = 2, exclude.zero = FALSE)

Arguments

m1 frequency matrix of motif 1
m2 frequency matrix of motif 2
min.align minimal number of basepairs that need to align
exclude.zero if to exclude offset=0, useful for calculating self-similarity

Details

The correlation score is essentially the sum of correlations of individual aligned columns as described in Pietrokovski (1996).

Value

single maximal score

References

useBigMemoryPWMEnrich  If to use a faster implementation of motif scanning that requires about 5 to 10 times more memory

Description
If to use a faster implementation of motif scanning that requires about 5 to 10 times more memory

Usage
useBigMemoryPWMEnrich(useBigMemory = FALSE)

Arguments
useBigMemory  a boolean value denoting if to use big memory implementation

Examples
## Not run:
useBigMemoryPWMEnrich(TRUE)  # switch to big memory implementation globally
useBigMemoryPWMEnrich(FALSE)  # switch back to default implementation
## End(Not run)

[,PWMBackground-method
Get the background for a subset of PWMs

Description
Get the background for a subset of PWMs

Usage
## S4 method for signature 'PWMBackground'
x[i, j, ..., drop = TRUE]

Arguments
x        the PWMBackground object
i        the indices of PWMs
j        unused
...      unused
drop     unused
Description
Get the background for a subset of PWMs

Usage
## S4 method for signature 'PWMEmpiricalBackground'
x[i, j, ..., drop = TRUE]

Arguments
- x: the PWMEmpiricalBackground object
- i: the indicies of PWMs
- j: unused
- ...: unused
- drop: unused

Description
Get the background for a subset of PWMs

Usage
## S4 method for signature 'PWMGEVBackground'
x[i, j, ..., drop = TRUE]

Arguments
- x: the PWMGEVBackground object
- i: the indicies of PWMs
- j: unused
- ...: unused
- drop: unused
Get the background for a subset of PWMs

Usage

### S4 method for signature 'PWMLognBackground'

```r
x[i, j, ..., drop = TRUE]
```

Arguments

- `x`: the PWMLognBackground object
- `i`: the indicies of PWMs
- `j`: unused
- `...`: unused
- `drop`: unused
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