# Package 'universalmotif'

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Title Import, Modify, and Export Motifs with R

**Version** 1.20.0

URL https://bioconductor.org/packages/universalmotif/

BugReports https://github.com/bjmt/universalmotif/issues

**Description** Allows for importing most common motif types into R for use by functions provided by other Bioconductor motif-related packages. Motifs can be exported into most major motif formats from various classes as defined by other Bioconductor packages. A suite of motif and sequence manipulation and analysis functions are included, including enrichment, comparison, P-value calculation, shuffling, trimming, higher-order motifs, and others.

**Depends** R (>= 3.5.0)

License GPL-3

**Encoding UTF-8** 

Imports methods, stats, utils, MASS, ggplot2, yaml, IRanges, Rcpp, Biostrings, BiocGenerics, S4Vectors, rlang, grid, MatrixGenerics

**Suggests** spelling, knitr, bookdown, TFBSTools, rmarkdown, MotifDb, testthat, BiocParallel, seqLogo, motifStack, dplyr, ape, ggtree, processx, ggseqlogo, cowplot, GenomicRanges, ggbio

Enhances PWMEnrich, rGADEM

LinkingTo Rcpp, RcppThread

VignetteBuilder knitr

biocViews MotifAnnotation, MotifDiscovery, DataImport, GeneRegulation

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```
'make_DBscores.R' 'merge_motifs.R' 'merge_similar.R'
      'motif_clusters.R' 'motif_finder.R' 'motif_peaks.R'
      'motif_pvalue.R' 'motif_rc.R' 'motif_tree.R' 'read_cisbp.R'
      'read_homer.R' 'read_jaspar.R' 'read_matrix.R' 'read_meme.R'
      'read_motifs.R' 'read_transfac.R' 'read_uniprobe.R'
      'run_meme.R' 'sample_sites.R' 'scan_sequences.R'
      'sequence_complexity.R' 'shuffle_motifs.R'
      'shuffle_sequences.R' 'switch_alph.R' 'trim_motifs.R'
      'universalmotif-methods.R' 'universalmotif.R'
      'universalmotif_df.R' 'utils-internal.R' 'utils-motif.R'
      'utils-sequence.R' 'view_logo.R' 'view_motifs.R'
      'write_homer.R' 'write_jaspar.R' 'write_matrix.R'
      'write_meme.R' 'write_motifs.R' 'write_transfac.R' 'zzz.R'
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```

# **R** topics documented:

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enrich_motifs
examplemotif
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# Description

If the original sequences are available for a particular motif, then they can be used to generate higher-order PPM matrices. See the "Motif import, export, and manipulation" vignette for more information.

4 add\_multifreq

#### Usage

```
add_multifreq(motif, sequences, add.k = 2:3, RC = FALSE,
   threshold = 0.001, threshold.type = "pvalue", motifs.perseq = 1,
   add.bkg = FALSE)
```

# Arguments

motif See convert\_motifs() for acceptable formats. If the motif is not a univer-

salmotif motif, then it will be converted.

sequences XStringSet The alphabet must match that of the motif. If these sequences are

all the same length as the motif, then they are all used to generate the multi-freq matrices. Otherwise scan\_sequences() is first run to find the best sequence

stretches within these.

add.k numeric(1) The k-let lengths to add.

RC logical(1) If TRUE, check reverse complement of the input sequences. Only

available for DNA/RNA.

threshold numeric(1) See details.

threshold.type character(1) One of c('pvalue', 'qvalue', 'logodds', 'logodds.abs').

See details.

motifs.perseq numeric(1) If scan\_sequences() is run, then this indicates how many hits

from each sequence is to be used.

add.bkg logical(1) Indicate whether to add corresponding higher order background

information to the motif. Can sometimes be detrimental when the input consists of few short sequences, which can increase the likelihood of adding zero or

near-zero probabilities.

# Details

See scan\_sequences() for more info on scanning parameters.

At each position in the motif, then the probability of each k-let covering from the initial position to ncol - 1 is calculated. Only positions within the motif are considered: this means that the final k-let probability matrix will have ncol - 1 fewer columns. Calculating k-let probabilities for the missing columns would be trivial however, as you would only need the background frequencies. Since these would not be useful for scan\_sequences() though, they are not calculated.

Currently add\_multifreq() does not try to stay faithful to the default motif matrix when generating multifreq matrices. This means that if the sequences used for training are completely different from the actual motif, the multifreq matrices will be as well. However this is only really a problem if you supply add\_multifreq() with a set of sequences of the same length as the motif. In this case add\_multifreq() is forced to create the multifreq matrices from these sequences. Otherwise add\_multifreq() will scan the input sequences for the motif and use the best matches to construct the multifreq matrices.

This 'multifreq' representation is only really useful within the **universalmotif** environment. Despite this, if you wish it can be preserved in text using write\_motifs().

ArabidopsisMotif 5

### A note on motif size:

The number of rows for each k-let matrix is n^k, with n being the number of letters in the alphabet being used. This means that the size of the k-let matrix can become quite large as k increases. For example, if one were to wish to represent a DNA motif of length 10 as a 10-let, this would require a matrix with 1,048,576 rows (though at this point if what you want is to search for exact sequence matches, the motif format itself is not very useful).

#### Value

A universalmotif object with filled multifreq slot. The bkg slot is also expanded with corresponding higher order probabilities if add.bkg = TRUE.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
scan_sequences(), convert_motifs(), write_motifs()
```

# **Examples**

```
sequences <- create_sequences(seqlen = 10)
motif <- create_motif()
motif.trained <- add_multifreq(motif, sequences, add.k = 2:4)
## peek at the 2-let matrix:
motif.trained["multifreq"]$`2`</pre>
```

ArabidopsisMotif

Arabidopsis motif in universalmotif format.

# Description

Arabidopsis motif trained from ArabidopsisPromoters using MEME version 4. This motif was generated at the command line using the following command: meme promoters.fa -revcomp -nmotifs 3 -mod anr -dna.

### Usage

ArabidopsisMotif

# **Format**

universalmotif

ArabidopsisPromoters Arabidopsis promoters as a DNAStringSet.

# **Description**

50 Arabidopsis promoters, each 1000 bases long. See the "Sequence manipulation and scanning" vignette for an example workflow describing extracting promoter sequences.

# Usage

ArabidopsisPromoters

## **Format**

DNAStringSet

compare\_motifs

Compare motifs.

# Description

Compare motifs using one of the several available metrics. See the "Motif comparisons and P-values" vignette for detailed information.

# Usage

```
compare_motifs(motifs, compare.to, db.scores, use.freq = 1,
  use.type = "PPM", method = "PCC", tryRC = TRUE, min.overlap = 6,
  min.mean.ic = 0.25, min.position.ic = 0, relative_entropy = FALSE,
  normalise.scores = FALSE, max.p = 0.01, max.e = 10, nthreads = 1,
  score.strat = "a.mean", output.report, output.report.max.print = 10)
```

# **Arguments**

motifs	See convert_motifs() for acceptable motif formats.
compare.to	numeric If missing, compares all motifs to all other motifs. Otherwise compares all motifs to the specified $motif(s)$ .
db.scores	data.frame or DataFrame. See details.
use.freq	numeric(1). For comparing the multifreq slot.
use.type	character(1) One of 'PPM' and 'ICM'. The latter allows for taking into account the background frequencies if relative_entropy = TRUE. Note that 'ICM' is not allowed when method = c("ALLR", "ALLR_LL").
method	character(1) One of PCC, EUCL, SW, KL, ALLR, BHAT, HELL, SEUCL, MAN, ALLR_LL, WEUCL, WPCC. See details.

tryRC logical(1) Try the reverse complement of the motifs as well, report the best

score.

min.overlap numeric(1) Minimum overlap required when aligning the motifs. Setting this to a number higher then the width of the motifs will not allow any overhangs.

Can also be a number between 0 and 1, representing the minimum fraction that

the motifs must overlap.

min.mean.ic numeric(1) Minimum mean information content between the two motifs for

an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="https://average\_ic()">average\_ic()</a> to filter out low IC motifs to get around this if you want to avoid

getting NAs in your output.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help punish scores resulting from only a fraction of an alignment.

relative\_entropy

logical(1) Change the ICM calculation affecting min.position.ic and min.mean.ic. See convert\_type().

normalise.scores

logical(1) Favour alignments which leave fewer unaligned positions, as well as alignments between motifs of similar length. Similarity scores are multiplied by the ratio of aligned positions to the total number of positions in the larger

motif, and the inverse for distance scores.

max.p numeric(1) Maximum P-value allowed in reporting matches. Only used if

compare. to is set.

max.e numeric(1) Maximum E-value allowed in reporting matches. Only used if

compare.to is set. The E-value is the P-value multiplied by the number of

input motifs times two.

nthreads numeric(1) Run compare\_motifs() in parallel with nthreads threads. nthreads

= 0 uses all available threads.

score.strat character(1) How to handle column scores calculated from motif alignments.

"sum": add up all scores. "a.mean": take the arithmetic mean. "g.mean": take the geometric mean. "median": take the median. "wa.mean", "wg.mean": weighted arithmetic/geometric mean. "fzt": Fisher Z-transform. Weights are the

total information content shared between aligned columns.

output.report character(1) Provide a filename for compare\_motifs() to write an html ouput

report to. The top matches are shown alongside figures of the match alignments.

This requires the knitr and rmarkdown packages. (Note: still in development.)

output.report.max.print

numeric(1) Maximum number of top matches to print.

### **Details**

### **Available metrics:**

The following metrics are available:

- Euclidean distance (EUCL) (Choi et al. 2004)
- Weighted Euclidean distance (WEUCL)
- Kullback-Leibler divergence (KL) (Kullback and Leibler 1951; Roepcke et al. 2005)
- Hellinger distance (HELL) (Hellinger 1909)
- Squared Euclidean distance (SEUCL)
- Manhattan distance (MAN)
- Pearson correlation coefficient (PCC)
- Weighted Pearson correlation coefficient (WPCC)
- Sandelin-Wasserman similarity (SW), or sum of squared distances (Sandelin and Wasserman 2004)
- Average log-likelihood ratio (ALLR) (Wang and Stormo 2003)
- Lower limit ALLR (ALLR\_LL) (Mahony et al. 2007)
- Bhattacharyya coefficient (BHAT) (Bhattacharyya 1943)

Comparisons are calculated between two motifs at a time. All possible alignments are scored, and the best score is reported. In an alignment scores are calculated individually between columns. How those scores are combined to generate the final alignment scores depends on score.strat.

See the "Motif comparisons and P-values" vignette for a description of the various metrics. Note that PCC, WPCC, SW, ALLR, ALLR\_LL and BHAT are similarities; higher values mean more similar motifs. For the remaining metrics, values closer to zero represent more similar motifs.

Small pseudocounts are automatically added when one of the following methods is used: KL, ALLR\_LL, IS. This is avoid zeros in the calculations.

### **Calculating P-values:**

To note regarding p-values: P-values are pre-computed using the make\_DBscores() function. If not given, then uses a set of internal precomputed P-values from the JASPAR2018 CORE motifs. These precalculated scores are dependent on the length of the motifs being compared. This takes into account that comparing small motifs with larger motifs leads to higher scores, since the probability of finding a higher scoring alignment is higher.

The default P-values have been precalculated for regular DNA motifs. They are of little use for motifs with a different number of alphabet letters (or even the multifreq slot).

# Value

matrix if compare.to is missing; DataFrame otherwise. For the latter, function args are stored in the metadata slot.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### References

Bhattacharyya A (1943). "On a measure of divergence between two statistical populations defined by their probability distributions." *Bulletin of the Calcutta Mathematical Society*, **35**, 99-109.

Choi I, Kwon J, Kim S (2004). "Local feature frequency profile: a method to measure structural similarity in proteins." *PNAS*, **101**, 3797-3802.

Hellinger E (1909). "Neue Begrundung der Theorie quadratischer Formen von unendlichvielen Veranderlichen." *Journal fur die reine und angewandte Mathematik*, **136**, 210-271.

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Mahony S, Auron PE, Benos PV (2007). "DNA Familial Binding Profiles Made Easy: Comparison of Various Motif Alignment and Clustering Strategies." *PLoS Computational Biology*, **3**.

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Roepcke S, Grossmann S, Rahmann S, Vingron M (2005). "T-Reg Comparator: an analysis tool for the comparison of position weight matrices." *Nucleic Acids Research*, **33**, W438-W441.

Sandelin A, Wasserman WW (2004). "Constrained binding site diversity within families of transcription factors enhances pattern discovery bioinformatics." *Journal of Molecular Biology*, **338**, 207-215.

Wang T, Stormo GD (2003). "Combining phylogenetic data with co-regulated genes to identify motifs." *Bioinformatics*, **19**, 2369-2380.

### See Also

```
convert_motifs(), motif_tree(), view_motifs(), make_DBscores()
```

## **Examples**

```
motif1 <- create_motif(name = "1")</pre>
motif2 <- create_motif(name = "2")</pre>
motif1vs2 <- compare_motifs(c(motif1, motif2), method = "PCC")</pre>
## To get a dist object:
as.dist(1 - motif1vs2)
motif3 <- create_motif(name = "3")</pre>
motif4 <- create_motif(name = "4")</pre>
motifs <- c(motif1, motif2, motif3, motif4)</pre>
## Compare motif "2" to all the other motifs:
if (R.Version()$arch != "i386") {
compare_motifs(motifs, compare.to = 2, max.p = 1, max.e = Inf)
## If you are working with a large list of motifs and the mean.min.ic
## option is not set to zero, you may get a number of failed comparisons
## due to low IC. To filter the list of motifs to avoid these, use
## the average_ic() function to remove motifs with low average IC:
## Not run:
```

```
library(MotifDb)
motifs <- convert_motifs(MotifDb)[1:100]
compare_motifs(motifs)
#> Warning in compare_motifs(motifs) :
#> Some comparisons failed due to low IC
motifs <- motifs[average_ic(motifs) > 0.5]
compare_motifs(motifs)
## End(Not run)
```

convert\_motifs

Convert motif class.

# **Description**

Allows for easy transfer of motif information between different classes as defined by other Bioconductor packages. This function is also used by nearly all other functions in this package, so any motifs of a compatible class can be used without needing to be converted beforehand.

#### Usage

```
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'AsIs'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'list'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'universalmotif'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'MotifList'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'TFFMFirst'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'PFMatrix'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'PWMatrix'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'ICMatrix'
convert_motifs(motifs, class = "universalmotif-universalmotif")
```

```
## S4 method for signature 'XMatrixList'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'pwm'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'pcm'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'pfm'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'PWM'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'Motif'
convert_motifs(motifs, class = "universalmotif-universalmotif")
## S4 method for signature 'matrix'
convert_motifs(motifs, class = "universalmotif-universalmotif")
```

#### **Arguments**

motifs Single motif object or list. See details.

class character(1) Desired motif class. Input as 'package-class'. If left empty, defaults to 'universalmotif-universalmotif'. (See details.)

# **Details**

#### Input

The following packge-class combinations can be used as input:

- MotifDb-MotifList
- TFBSTools-PFMatrix
- TFBSTools-PWMatrix
- TFBSTools-ICMatrix
- TFBSTools-PFMatrixList
- TFBSTools-PWMatrixList
- TFBSTools-ICMatrixList
- TFBSTools-TFFMFirst
- seqLogo-pwm
- motifStack-pcm
- motifStack-pfm
- PWMEnrich-PWM
- motifRG-Motif
- universalmotif-universalmotif

• matrix

#### **Output:**

The following package-class combinations can be output:

- MotifDb-MotifList
- TFBSTools-PFMatrix
- TFBSTools-PWMatrix
- TFBSTools-ICMatrix
- TFBSTools-TFFMFirst
- seqLogo-pwm
- motifStack-pcm
- · motifStack-pfm
- PWMEnrich-PWM
- Biostrings-PWM (type = 'log2prob')
- rGADEM-motif
- universalmotif-universalmotif (the default, no need to specify this)

Note: MotifDb-MotifList output was a later addition to <code>convert\_motifs()</code>. As a result, to stay consistent with previous behaviour most functions will always convert MotifDb-MotifList objects to a list of universalmotif motifs, even if other formats would be simply returned as is (e.g. for other formats, <code>filter\_motifs()</code> will return the input format; for MotifDb-MotifList, a list of universalmotif objects will be returned).

#### Value

Single motif object or list.

#### Methods (by class)

- AsIs: Generate an error to remind users to run to\_list() instead of using the column from to\_df() directly.
- list: Convert a list of motifs.
- universalmotif: Convert a universalmotif object.
- MotifList: Convert MotifList motifs. (MotifDb)
- TFFMFirst: Convert TFFMFirst motifs. (TFBSTools)
- PFMatrix: Convert PFMatrix motifs. (TFBSTools)
- PWMatrix: Convert PWMatrix motifs. (TFBSTools)
- ICMatrix: Convert ICMatrix motifs. (TFBSTools)
- XMatrixList: Convert XMatrixList motifs. (TFBSTools)
- pwm: Convert pwm motifs. (**seqLogo**)
- pcm: Convert pcm motifs. (motifStack)
- pfm: Convert pfm motifs. (motifStack)
- PWM: Convert PWM motifs. (**PWMEnrich**)
- Motif: Convert Motif motifs. (motifRG)
- matrix: Create motif from matrices.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Bembom O (2018). seqLogo: Sequence logos for DNA sequence alignments. R package version 1.46.0.

Droit A, Gottardo R, Robertson G, Li L (2014). rGADEM: de novo motif discovery. R package version 2.28.0.

Mercier E, Gottardo R (2014). *MotIV: Motif Identification and Validation*. R package version 1.36.0.

Ou J, Wolfe SA, Brodsky MH, Zhu LJ (2018). "motifStack for the analysis of transcription factor binding site evolution." *Nature Methods*, **15**, 8-9. doi: 10.1038/nmeth.4555.

Shannon P, Richards M (2018). *MotifDb: An Annotated Collection of Protein-DNA Binding Sequence Motifs*. R package version 1.22.0.

Stojnic R, Diez D (2015). PWMEnrich: PWM enrichment analysis. R package version 4.16.0.

Tan G, Lenhard B (2016). "TFBSTools: an R/Bioconductor package for transcription factor binding site analysis." *Bioinformatics*, **32**, 1555-1556. doi: 10.1093/bioinformatics/btw024.

Yao Z (2012). motifRG: A package for discriminative motif discovery, designed for high throughput sequencing dataset. R package version 1.24.0.

#### **Examples**

```
# Convert from universalmotif:
jaspar <- read_jaspar(system.file("extdata", "jaspar.txt",</pre>
                                   package = "universalmotif"))
if (requireNamespace("motifStack", quietly = TRUE)) {
  jaspar.motifstack.pfm <- convert_motifs(jaspar, "motifStack-pfm")</pre>
}
# Convert from another class to universalmotif:
if (requireNamespace("TFBSTools", quietly = TRUE)) {
library(TFBSTools)
data(MA0003.2)
motif <- convert_motifs(MA0003.2)</pre>
# Convert from another class to another class
if (requireNamespace("PWMEnrich", quietly = TRUE)) {
  motif <- convert_motifs(MA0003.2, "PWMEnrich-PWM")</pre>
# The 'convert_motifs' function is embedded in the rest of the universalmotif
# functions: non-universalmotif class motifs can be used
MA0003.2.trimmed <- trim_motifs(MA0003.2)
# Note: if the motif object going in has information that the
# 'universalmotif' class can't hold, it will be lost
```

14 convert\_type

convert\_type

Convert universalmotif type.

## **Description**

Switch between position count matrix (PCM), position probability matrix (PPM), position weight matrix (PWM), and information count matrix (ICM) types. See the "Introduction to sequence motifs" vignette for details. Please also note that type conversion occurs implicitly throughout the universalmotif package, so there is generally no need to perform this manual conversion. Also please be aware that the message concerning pseudocount-adjusting motifs can be disabled via options(pseudocount.warning=FALSE).

# Usage

```
convert_type(motifs, type, pseudocount, nsize_correction = FALSE,
  relative_entropy = FALSE)
```

# **Arguments**

motifs See convert\_motifs() for acceptable formats.

type character(1) One of c('PCM', 'PPM', 'PWM', 'ICM').

pseudocount numeric(1) Correction to be applied to prevent -Inf from appearing in PWM

matrices. If missing, the pseudocount stored in the universalmotif 'pseudocount'

slot will be used.

nsize\_correction

logical(1) If true, the ICM at each position will be corrected to account for

small sample sizes. Only used if relative\_entropy = FALSE.

relative\_entropy

logical(1) If true, the ICM will be calculated as relative entropy. See details.

# **Details**

# PCM:

Position count matrix (PCM), also known as position frequency matrix (PFM). For n sequences from which the motif was built, each position is represented by the numbers of each letter at that position. In theory all positions should have sums equal to n, but not all databases are this consistent. If converting from another type to PCM, column sums will be equal to the 'nsites' slot. If empty, 100 is used.

## PPM:

Position probability matrix (PPM), also known as position frequency matrix (PFM). At each position, the probability of individual letters is calculated by dividing the count for that letter by the total sum of counts at that position (letter\_count / position\_total). As a result, each position will sum to 1. Letters with counts of 0 will thus have a probability of 0, which can be undesirable when searching for motifs in a set of sequences. To avoid this a pseudocount can be added ((letter\_count + pseudocount)) / (position\_total + pseudocount)).

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#### PWM:

Position weight matrix (PWM; Stormo et al. (1982)), also known as position-specific weight matrix (PSWM), position-specific scoring matrix (PSSM), or log-odds matrix. At each position, each letter is represented by it's log-likelihood (log2(letter\_probability / background\_probility)), which is normalized using the background letter frequencies. A PWM matrix is constructed from a PPM. If any position has 0-probability letters to which pseudocounts were not added, then the final log-likelihood of these letters will be -Inf.

#### ICM:

Information content matrix (ICM; Schneider and Stephens 1990). An ICM is a PPM where each letter probability is multiplied by the total information content at that position. The information content of each position is determined as: totalIC - Hi, where the total information totalIC totalIC <- log2(alphabet\_length), and the Shannon entropy (Shannon 1948) for a specific position (Hi)

 $Hi \leftarrow -sum(sapply(alphabet\_frequencies, function(x) x * log(2)).$ 

As a result, the total sum or height of each position is representative of it's sequence conservation, measured in the unit 'bits', which is a unit of energy (Schneider 1991; see <a href="https://fr-s-schneider.ncifcrf.gov/logorecommendations.html">https://fr-s-schneider.ncifcrf.gov/logorecommendations.html</a> for more information). However not all programs will calculate information content the same. Some will 'correct' the total information content at each position using a correction factor as described by Schneider et al. (1986). This correction can applied by setting nsize\_correction = TRUE, however it will only be applied if the 'nsites' slot is not empty. This is done using TFBSTools:::schneider\_correction (Tan and Lenhard 2016). As such, converting from an ICM to which some form of correction has been applied will result in a PCM/PPM/PWM with slight inaccuracies.

Another method of calculating information content is calculating the relative entropy, also known as Kullback-Leibler divergence (Kullback and Leibler 1951). This accounts for background frequencies, which can be useful for genomes with a heavy imbalance in letter frequencies. For each position, the individual letter frequencies are calculated as letter\_freq \* log2(letter\_freq / bkg\_freq). When calculating information content using Shannon entropy, the maximum content for each position will always be log2(alphabet\_length). This does not hold for information content calculated as relative entropy. Please note that conversion from ICM assumes the information content was *not* calculated as relative entropy.

### Value

See convert\_motifs() for possible output motif objects.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

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#### See Also

```
convert_motifs()
```

# **Examples**

create\_motif

Create a motif.

## **Description**

Create a motif from a set of sequences, a matrix, or generate a random motif. See the "Motif import, export and manipulation" vignette for details.

# Usage

```
create_motif(input, alphabet, type = "PPM", name = "motif",
   pseudocount = 0, bkg, nsites, altname, family, organism, bkgsites, strand,
   pval, qval, eval, extrainfo, add.multifreq)

## S4 method for signature 'missing'
create_motif(input, alphabet, type = "PPM",
```

```
name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'numeric'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'character'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'matrix'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'DNAStringSet'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'RNAStringSet'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'AAStringSet'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
 bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
## S4 method for signature 'BStringSet'
create_motif(input, alphabet, type = "PPM",
  name = "motif", pseudocount = 0, bkg, nsites, altname, family, organism,
  bkgsites, strand, pval, qval, eval, extrainfo, add.multifreq)
```

# **Arguments**

input character, numeric, matrix, XStringSet, or missing.

alphabet character(1) One of c('DNA', 'RNA', 'AA'), or a combined string represent-

ing the letters. If no alphabet is provided then it will try and guess the alphabet

from the input.

type character(1) One of c('PCM', 'PPM', 'PWM', 'ICM').

name character(1) Motif name.

pseudocount numeric(1) Correction to be applied to prevent -Inf from appearing in PWM

matrices. Defaults to 0.

numeric A vector of probabilities, each between 0 and 1. If higher order backbkg grounds are provided, then the elements of the vector must be named. If unnamed, then the order of probabilities must be in the same order as the alphabetically sorted sequence alphabet. nsites numeric(1) Number of sites the motif was constructed from. If blank, then create\_motif() will guess the appropriate number if possible. To prevent this, provide nsites = numeric(). altname character(1) Alternate motif name. family character(1) Transcription factor family. organism character(1) Species of origin. bkgsites numeric(1) Total number of sites used to find the motif. character(1) Whether the motif is specific to a certain strand. Acceptable strand strands are '+', '-', and '+-' (to represent both strands). Note that '-+' and '\*' can also be provided to represent both strands, but the final strand in the universalmotif object will be set to '+-'. numeric(1) P-value associated with motif. pval qval numeric(1) Adjusted P-value associated with motif. eval numeric(1) E-value associated with motif. extrainfo character Any other extra information, represented as a named character vecadd.multifreq numeric If the motif is created from a set of sequences, then the add\_multifreq() function can be run at the same time (with RC = FALSE).

#### **Details**

The aim of this function is provide an easy interface to creating universalmotif motifs, as an alternative to the default class constructor (i.e. new('universalmotif', name=...)). See examples for potential use cases.

Note: when generating random motifs, the nsites slot is also given a random value.

See the examples section for more info on motif creation.

#### Value

universalmotif object.

# Methods (by class)

- missing: Create a random motif of length 10.
- numeric: Create a random motif with a specified length.
- character: Create motif from a consensus string.
- matrix: Create motif from a matrix.
- DNAStringSet: Create motif from a DNAStringSet.
- RNAStringSet: Create motif from a RNAStringSet.
- AAStringSet: Create motif from a AAStringSet.
- BStringSet: Create motif from a BStringSet.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
convert_type(), add_multifreq(), create_sequences(), shuffle_motifs().
```

### **Examples**

```
##### create motifs from a single string
# Motif is by default generated as a PPM: change final type as desired
DNA.motif <- create_motif("TATAWAW")</pre>
DNA.motif <- create_motif("TATAWAW", type = "PCM")
# Nsites will be set to the number of input sequences unless specified or
# a single string is used as input
DNA.motif <- create_motif("TTTTTTT", nsites = 10)</pre>
# Ambiguity letters can be used:
DNA.motif <- create_motif("TATAWAW")</pre>
DNA.motif <- create_motif("NNVVWWAAWWDDN")</pre>
# Be careful about setting nsites when using ambiguity letters!
DNA.motif <- create_motif("NNVVWWAAWWDDN", nsites = 1)</pre>
RNA.motif <- create_motif("UUUCCG")</pre>
# 'create_motif' will try to detect the alphabet type; this can be
# unreliable for AA and custom alphabets as DNA and RNA alphabets are
# detected first
AA.motif <- create_motif("AVLK", alphabet = "AA")
custom.motif <- create_motif("QWER", alphabet = "QWER")</pre>
# Specify custom alphabet
custom.motif <- create_motif("QWER", alphabet = "QWERASDF")</pre>
###### Create motifs from multiple strings of equal length
DNA.motif <- create_motif(c("TTTT", "AAAA", "AACC", "TTGG"), type = "PPM")</pre>
DNA.motif <- create_motif(c("TTTT", "AAAA", "AACC", "TTGG"), nsites = 20)</pre>
RNA.motif <- create_motif(c("UUUU", "AAAA", "AACC", "UUGG"), type = "PWM")</pre>
AA.motif <- create_motif(c("ARNDCQ", "EGHILK", "ARNDCQ"), alphabet = "AA")
custom.motif <- create_motif(c("POIU", "LKJH", "POIU", "CVBN"),</pre>
                              alphabet = "POIULKJHCVBN")
# Ambiguity letters are only allowed for single consensus strings: the
# following fails
## Not run:
create_motif(c("WWTT", "CCGG"))
create_motif(c("XXXX", "XXXX"), alphabet = "AA")
```

```
## End(Not run)
##### Create motifs from XStringSet objects
library(Biostrings)
DNA.set <- DNAStringSet(c("TTTT", "AAAA", "AACC", "TTGG"))</pre>
DNA.motif <- create_motif(DNA.set)</pre>
RNA.set <- RNAStringSet(c("UUUU", "AACC", "UUCC"))</pre>
RNA.motif <- create_motif(RNA.set)</pre>
AA.set <- AAStringSet(c("VVVLLL", "AAAIII"))
AA.motif <- create_motif(AA.set)
# Custom motifs can be created from BStringSet objects
B.set <- BStringSet(c("QWER", "ASDF", "ZXCV", "TYUI"))</pre>
custom.motif <- create_motif(B.set)</pre>
##### Create motifs with filled 'multifreq' slot
DNA.motif.k2 <- create_motif(DNA.set, add.multifreq = 2)
##### Create motifs from matrices
mat <- matrix(c(1, 1, 1, 1,
                 2, 0, 2, 0,
                 0, 2, 0, 2,
                 0, 0, 0, 0),
                 nrow = 4, byrow = TRUE)
DNA.motif <- create_motif(mat, alphabet = "DNA")</pre>
RNA.motif <- create_motif(mat, alphabet = "RNA", nsites = 20)</pre>
custom.motif <- create_motif(mat, alphabet = "QWER")</pre>
# Specify custom alphabet
custom.motif <- create_motif(mat, alphabet = "QWER")</pre>
# Alphabet can be detected from rownames
rownames(mat) <- DNA_BASES</pre>
DNA.motif <- create_motif(mat)</pre>
rownames(mat) <- c("Q", "W", "E", "R")
custom.motif <- create_motif(mat)</pre>
# Matrices can also be used as input
mat.ppm \leftarrow matrix(c(0.1, 0.1, 0.1, 0.1,
                     0.5, 0.5, 0.5, 0.5,
                     0.1, 0.1, 0.1, 0.1,
                     0.3, 0.3, 0.3, 0.3),
                     nrow = 4, byrow = TRUE)
DNA.motif <- create_motif(mat.ppm, alphabet = "DNA", type = "PPM")
##### Create random motifs
# These are generated as PPMs with 10 positions
```

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```
DNA.motif <- create_motif()
RNA.motif <- create_motif(alphabet = "RNA")
AA.motif <- create_motif(alphabet = "AA")
custom.motif <- create_motif(alphabet = "QWER")

# The number of positions can be specified

DNA.motif <- create_motif(5)

# If the background frequencies are not provided, they are generated # using `rpois`; positions are created using `rdirichlet(1, bkg)`.
# (calling `create_motif()` creates motifs with an average # positional IC of 1)

DNA.motif <- create_motif(bkg = c(0.3, 0.2, 0.2, 0.3))
DNA.motif <- create_motif(10, bkg = c(0.1, 0.4, 0.4, 0.1))</pre>
```

create\_sequences

Create random sequences.

## **Description**

Generate random sequences from any set of characters, represented as XStringSet objects.

# Usage

```
create_sequences(alphabet = "DNA", seqnum = 100, seqlen = 100, freqs,
  nthreads = 1, rng.seed = sample.int(10000, 1))
```

### **Arguments**

alphabet	character(1) One of c('DNA', 'RNA', 'AA'), or a string of characters to be used as the alphabet.
seqnum	numeric(1) Number of sequences to generate.
seqlen	numeric(1) Length of random sequences.
freqs	numeric A named vector of probabilities. The length of the vector must be the power of the number of letters in the sequence alphabet. Probabilities can only be provided for a single size k.
nthreads	<pre>numeric(1) Run create_sequences() in parallel with nthreads threads. nthreads = 0 uses all available threads. Note that no speed up will occur for jobs with seqnum = 1.</pre>
rng.seed	numeric(1) Set random number generator seed. Since sequence creation can occur simultaneously in multiple threads using C++, it cannot communicate with the regular R random number generator state and thus requires an independent seed. Each individual sequence creation instance is given the following

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seed: rng.seed \* index. The default is to pick a random number as chosen by sample(), which effectively is making create\_sequences() dependent on the R RNG state.

#### Value

XStringSet The returned sequences are *unnamed*.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
create_motif(), shuffle_sequences()
```

## **Examples**

```
## Create DNA sequences with slightly increased AT content:
sequences <- create_sequences(freqs = c(A=0.3, C=0.2, G=0.2, T=0.3))
## Create custom sequences:
sequences.QWER <- create_sequences("QWER")
## You can include non-alphabet characters are well, even spaces:
sequences.custom <- create_sequences("!@#$ ")</pre>
```

enrich\_motifs

Enrich for input motifs in a set of sequences.

# Description

Given a set of target and background sequences, test if the input motifs are significantly enriched in the targets sequences relative to the background sequences. See the "Sequence manipulation and scanning" vignette.

### Usage

```
enrich_motifs(motifs, sequences, bkg.sequences, max.p = 0.001,
    max.q = 0.001, max.e = 0.001, qval.method = "fdr", threshold = 1e-04,
    threshold.type = "pvalue", verbose = 0, RC = TRUE, use.freq = 1,
    shuffle.k = 2, shuffle.method = "euler", return.scan.results = FALSE,
    nthreads = 1, rng.seed = sample.int(10000, 1), motif_pvalue.k = 8,
    use.gaps = TRUE, allow.nonfinite = FALSE, warn.NA = TRUE,
    no.overlaps = TRUE, no.overlaps.by.strand = FALSE,
    no.overlaps.strat = "score", respect.strand = FALSE,
    motif_pvalue.method = c("dynamic", "exhaustive"),
    scan_sequences.qvals.method = c("BH", "fdr", "bonferroni"),
    mode = c("total.hits", "seq.hits"), pseudocount = 1)
```

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#### **Arguments**

motifs See convert\_motifs() for acceptable motif formats. XStringSet Sequences to scan. Alphabet should match motif. seauences XStringSet Optional. If missing, shuffle\_sequences() is used to create bkg.sequences background sequences from the input sequences. numeric(1) P-value threshold. max.p numeric(1) Adjusted P-value threshold. This is only useful if multiple motifs max.q are being enriched for. numeric(1). The E-value is calculated by multiplying the P-value with the max.e number of input motifs times two (McLeay and Bailey 2010). gval.method character(1) See stats::p.adjust(). threshold numeric(1) See details. character(1) One of c('pvalue', 'qvalue', 'logodds', 'logodds.abs'). threshold.type See details. verbose numeric(1) 0 for no output, 4 for max verbosity. logical(1) If TRUE, check reverse complement of the input sequences. Only RC. available for DNA/RNA. numeric(1) The default, 1, uses the motif matrix (from the motif['motif'] use.freq slot) to search for sequences. If a higher number is used, then the matching k-let matrix from the motif['multifreq'] slot is used. See add\_multifreq(). shuffle.k numeric(1) The k-let size to use when shuffling input sequences. Only used if no background sequences are input. See shuffle\_sequences(). shuffle.method character(1) One of c('euler', 'markov', 'linear'). See shuffle\_sequences(). return.scan.results logical(1) Return output from scan\_sequences(). For large jobs, leaving this as FALSE can save a small amount time by preventing construction of the complete results data. frame from scan\_sequences(). nthreads numeric(1) Run scan\_sequences() in parallel with nthreads threads. nthreads = 0 uses all available threads. Note that no speed up will occur for jobs with only a single motif and sequence. numeric(1) Set random number generator seed. Since shuffling can occur sirng.seed multaneously in multiple threads using C++, it cannot communicate with the regular R random number generator state and thus requires an independent seed. Each individual sequence in an XStringSet object will be given the following seed: rng.seed \* index. See shuffle\_sequences(). motif\_pvalue.k numeric(1) Control motif\_pvalue() approximation. See motif\_pvalue(). use.gaps logical(1) Set this to FALSE to ignore motif gaps, if present. allow.nonfinite logical(1) If FALSE, then apply a pseudocount if non-finite values are found in the PWM. Note that if the motif has a pseudocount greater than zero and

> the motif is not currently of type PWM, then this parameter has no effect as the pseudocount will be applied automatically when the motif is converted to a

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> PWM internally. This value is set to FALSE by default in order to stay consistent with pre-version 1.8.0 behaviour. A message will be printed if a pseudocount is applied. To disable this, set options(pseudocount.warning=FALSE).

warn.NA

logical(1) Whether to warn about the presence of non-standard letters in the input sequence, such as those in masked sequences.

no.overlaps

logical(1) Remove overlapping hits from the same motifs. Overlapping hits from different motifs are preserved. Please note that the current implementation of this feature can add significantly to the run time for large inputs.

no.overlaps.by.strand

logical(1) Whether to discard overlapping hits from the opposite strand (TRUE), or to only discard overlapping hits on the same strand (FALSE).

no.overlaps.strat

character(1) One of c("score", "order"). The former option keeps the highest scoring overlapping hit (and the first of these within ties), and the latter simply keeps the first overlapping hit.

respect.strand logical(1) If motifs are DNA/RNA, then setting this option to TRUE will make scan\_sequences() only scan the strands of the input sequences as indicated in the motif strand slot.

motif\_pvalue.method

character(1) One of c("dynamic", "exhaustive"). Algorithm used for calculating P-values. The "exhaustive" method involves finding all possible motif matches at or above the specified score using a branch-and-bound algorithm, which can be computationally intensive (Hartman et al., 2013). Additionally, the computation must be repeated for each hit. The "dynamic" method calculates the distribution of possible motif scores using a much faster dynamic programming algorithm, and can be recycled for multiple scores (Grant et al., 2011). The only disadvantage is the inability to use allow.nonfinite = TRUE. See motif\_pvalue() for details.

scan\_sequences.qvals.method

character(1) One of c("fdr", "BH", "bonferroni"). The method for calculating adjusted P-values for individual motif hits. These are described in depth in the Sequence Searches vignette.

mode

character(1) One of c("total.hits", "seq.hits"). The former enriches for the total count of motif hits across all sequences, whereas the latter only counts motif hits once per sequence (useful for cases where there are many small sequences).

pseudocount

integer(1) Add a pseudocount to the motif hit counts when performing the Fisher test.

#### **Details**

To find enriched motifs, scan\_sequences() is run on both target and background sequences. stats::fisher.test() is run to test for enrichment.

See scan\_sequences() for more info on scanning parameters.

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# Value

DataFrame Enrichment results in a DataFrame. Function args and (optionally) scan results are stored in the metadata slot.

### Author(s)

Benjamin Jean-Marie Tremblay <br/> <br/> denjamin.tremblay@uwaterloo.ca>

#### References

McLeay R, Bailey TL (2010). "Motif Enrichment Analysis: A unified framework and method evaluation." *BMC Bioinformatics*, **11**.

### See Also

```
scan_sequences(), shuffle_sequences(), add_multifreq(), motif_pvalue()
```

# **Examples**

```
data(ArabidopsisPromoters)
data(ArabidopsisMotif)
if (R.Version()$arch != "i386") {
enrich_motifs(ArabidopsisMotif, ArabidopsisPromoters, threshold = 0.01)
}
```

examplemotif

Example motif in universalmotif format.

# **Description**

A simple DNA motif. To recreate this motif: create\_motif("TATAWAW", nsites = numeric())

# Usage

examplemotif

#### **Format**

universalmotif

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examplemotif2	Another example motif in universalmotif format.	

# Description

A simple DNA motif with a non-empty multifreq slot. To recreate to this motif:  $add_multifreq(examplemotif, DNAStringSet(rep(c("CAAAACC", "CTTTTCC"), 3)))$ 

# Usage

examplemotif2

### **Format**

universalmotif

filter\_motifs Filter a list of motifs.

# **Description**

Filter motifs based on the contents of available universalmotif slots. If the input motifs are not of universalmotif, then they will be converted for the duration of the filter\_motifs() operation.

# Usage

```
filter_motifs(motifs, name, altname, family, organism, width, alphabet, type,
icscore, nsites, strand, pval, qval, eval, extrainfo)
```

### **Arguments**

motifs	list See convert_motifs() for acceptable formats.
name	character Keep motifs by names.
altname	character Keep motifs by altnames.
family	character Keep motifs by family.
organism	character Keep motifs by organism.
width	numeric(1) Keep motifs with minimum width.
alphabet	character Keep motifs by alphabet.
type	character Keep motifs by type.
icscore	numeric(1) Keep motifs with minimum total IC.
nsites	$\label{prop:condition} numeric \mbox{(1) Keep motifs with minimum number of target sites.}$
strand	character Keeps motifs by strand.

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pval	numeric(1) Keep motifs by max P-value.
qval	numeric(1) Keep motifs by max Q-value.
eval	numeric(1) Keep motifs by max E-val.
extrainfo	character Named character vector of items that must be present in motif extrainfo slots.

### Value

list Motifs. An attempt will be made to preserve the original class, see convert\_motifs() for limitations.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### **Examples**

```
## By minimum IC:
jaspar <- read_jaspar(system.file("extdata", "jaspar.txt",</pre>
                                   package = "universalmotif"))
jaspar.ic3 <- filter_motifs(jaspar, icscore = 3)</pre>
## Starting from version 1.10.0 of the universalmotif package, one
## could instead make use of the universalmotif_df structure:
jaspar.ic3 <- jaspar |> to_df() |> subset(icscore > 3) |> to_list()
## By organism:
## Not run:
library(MotifDb)
motifs <- convert_motifs(MotifDb)</pre>
motifs <- filter_motifs(motifs, organism = c("Athaliana", "Mmusculus"),</pre>
                         extrainfo = c("dataSource" = "cisbp_1.02"))
motifs <- convert_motifs(MotifDb) |> to_df() |>
  subset(organism %in% c("Athaliana", "Mmusculus") &
    dataSource == "cisbp_1.02") |> to_list()
## End(Not run)
```

fontDFroboto

Polygon coordinates for plotting letters.

# **Description**

DataFrame of polygon coordinates used by view\_motifs() for plotting letters. It was generated using the createPolygons function from the gglogo package for the font Roboto Medium.

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#### Usage

fontDFroboto

#### **Format**

**DataFrame** 

get\_bkg

Calculate sequence background.

# **Description**

For a set of input sequences, calculate the overall sequence background for any k-let size. For very large sequences DNA and RNA sequences (in the billions of bases), please be aware of the much faster and more efficient Biostrings::oligonucleotideFrequency(). get\_bkg() can still be used in these cases, though it may take several seconds or minutes to calculate the results (depending on requested k-let sizes).

## Usage

```
get_bkg(sequences, k = 1:3, as.prob = NULL, pseudocount = 0,
    alphabet = NULL, to.meme = NULL, RC = FALSE, list.out = NULL,
    nthreads = 1, merge.res = TRUE, window = FALSE, window.size = 0.1,
    window.overlap = 0)
```

# **Arguments**

	MOLIT OF T	NT	
sequences	XStringSet Input sequences.	Note that if multiple sequences are present, the	ne

results will be combined into one (unless merge.res = FALSE).

k integer Size of k-let. Background can be calculated for any k-let size.

as.prob Deprecated.

pseudocount integer (1) Add a count to each possible k-let. Prevents any k-let from having

0 or 1 probabilities.

alphabet character(1) Provide a custom alphabet to calculate a background for. If NULL,

then standard letters will be assumed for DNA, RNA and AA sequences, and all unique letters found will be used for BStringSet type sequences. Note that letters which are not a part of the standard DNA/RNA/AA alphabets or in the provided alphabet will not be counted in the totals during probability calcula-

tions.

to.meme If not NULL, then get\_bkg() will return the sequence background in MEME

Markov Background Model format. Input for this argument will be used for cat(..., file = to.meme) within get\_bkg(). See http://meme-suite.org/

doc/bfile-format.html for a description of the format.

RC logical(1) Calculate the background of the reverse complement of the input

sequences as well. Only valid for DNA/RNA.

get\_bkg

list.out	Deprecated.
nthreads	$numeric(1)$ Run $get_bkg()$ in parallel with nthreads threads. nthreads = 0 uses all available threads. Note that no speed up will occur for jobs with only a single sequence.
merge.res	logical(1) Whether to merge results from all sequences or return background data for individual sequences.
window	logical(1) Determine background in windows.
window.size	numeric Window size. If a number between 0 and 1 is provided, the value is calculated as the number multiplied by the sequence length.
window.overlap	numeric Overlap between windows. If a number between 0 and 1 is provided, the value is calculated as the number multiplied by the sequence length.

#### Value

If to.meme = NULL, a DataFrame with columns klet, count, and probability. If merge.res = FALSE, there will be an additional sequence column. If window = TRUE, there will be an additional start and stop columns.

If to.meme is not NULL, then NULL is returned, invisibly.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Bailey TL, Elkan C (1994). "Fitting a mixture model by expectation maximization to discover motifs in biopolymers." *Proceedings of the Second International Conference on Intelligent Systems for Molecular Biology*, **2**, 28-36.

# See Also

```
create_sequences(), scan_sequences(), shuffle_sequences()
```

### **Examples**

```
## Compare to Biostrings version
library(Biostrings)
seqs.DNA <- create_sequences()
bkg.DNA <- get_bkg(seqs.DNA, k = 3)
bkg.DNA2 <- oligonucleotideFrequency(seqs.DNA, 3, 1, as.prob = FALSE)
bkg.DNA2 <- colSums(bkg.DNA2)
all(bkg.DNA$count == bkg.DNA2)

## Create a MEME background file
get_bkg(seqs.DNA, k = 1:3, to.meme = stdout(), pseudocount = 1)

## Non-DNA/RNA/AA alphabets
seqs.QWERTY <- create_sequences("QWERTY")
bkg.QWERTY <- get_bkg(seqs.QWERTY, k = 1:2)</pre>
```

30 make\_DBscores

JASPAR2018\_CORE\_DBSCORES

JASPAR2018 CORE database scores

# **Description**

For use with compare\_motifs(). The precomputed scores allow for fast P-value estimation. These scores were generated using make\_DBscores() with the JASPAR2018 CORE motif set. The scores are organized in a DataFrame. In this DataFrame is the location and scale of scores resulting from a statistical distribution using the the comparisons of JASPAR2018 CORE motifs with randomized motifs of the specified subject and target motif length. Created using make\_DBscores() from universalmotif v1.4.0. The parameters used can be seen via S4Vectors::metadata(JASPAR2018\_CORE\_DBSCORES).

#### **Usage**

JASPAR2018\_CORE\_DBSCORES

#### **Format**

DataFrame with function args in the metadata slot.

make\_DBscores

Create P-value databases.

# Description

Generate data used by compare\_motifs() for P-value calculations. By default, compare\_motifs() uses an internal database based on the JASPAR2018 core motifs (Khan et al. 2018). Parameters for distributions are are estimated for every combination of motif widths.

# Usage

```
make_DBscores(db.motifs, method = c("PCC", "EUCL", "SW", "KL", "WEUCL",
   "ALLR", "BHAT", "HELL", "WPCC", "SEUCL", "MAN", "ALLR_LL"),
   shuffle.db = TRUE, shuffle.k = 3, shuffle.method = "linear",
   rand.tries = 1000, widths = 5:30, min.position.ic = 0,
   normalise.scores = c(FALSE, TRUE), min.overlap = 6, min.mean.ic = 0.25,
   progress = TRUE, nthreads = 1, tryRC = TRUE, score.strat = c("sum",
   "a.mean", "g.mean", "median", "wa.mean", "wg.mean", "fzt"))
```

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#### **Arguments**

db.motifs list Database motifs.

method character(1) One of PCC, EUCL, SW, KL, ALLR, BHAT, HELL, SEUCL,

MAN, ALLR LL, WEUCL, WPCC. See details.

shuffle.db logical(1) Deprecated. Does nothing. generate random motifs with create\_motif().

shuffle.k numeric(1) See shuffle\_motifs().

shuffle.method character(1) See shuffle\_motifs().

rand.tries numeric(1) Approximate number of comparisons to perform for every combi-

nation of widths.

widths numeric Motif widths to use in P-value database calculation.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help punish scores resulting from only a fraction of an alignment.

normalise.scores

logical(1) Favour alignments which leave fewer unaligned positions, as well as alignments between motifs of similar length. Similarity scores are multiplied by the ratio of aligned positions to the total number of positions in the larger

motif, and the inverse for distance scores.

min.overlap numeric(1) Minimum overlap required when aligning the motifs. Setting this

to a number higher then the width of the motifs will not allow any overhangs. Can also be a number between 0 and 1, representing the minimum fraction that

the motifs must overlap.

min.mean.ic numeric(1) Minimum mean information content between the two motifs for

an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="https://example.com/article/a

getting NAs in your output.

progress logical(1) Show progress.

nthreads numeric(1) Run compare\_motifs() in parallel with nthreads threads. nthreads

= 0 uses all available threads.

tryRC logical(1) Try the reverse complement of the motifs as well, report the best

score.

score.strat character(1) How to handle column scores calculated from motif alignments.

"sum": add up all scores. "a.mean": take the arithmetic mean. "g.mean": take the geometric mean. "median": take the median. "wa.mean", "wg.mean": weighted arithmetic/geometric mean. "fzt": Fisher Z-transform. Weights are the

total information content shared between aligned columns.

# Details

See compare\_motifs() for more info on comparison parameters.

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To replicate the internal **universalmotif** DB scores, run make\_DBscores() with the default settings. Note that this will be a slow process.

Arguments widths, method, normalise.scores and score.strat are vectorized; all combinations will be attempted.

#### Value

A DataFrame with score distributions for the input database. If more than one make\_DBscores() run occurs (i.e. args method, normalise.scores or score.strat are longer than 1), then the function args are included in the metadata slot.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Khan A, Fornes O, Stigliani A, Gheorghe M, Castro-Mondragon JA, van der Lee R, Bessy A, Cheneby J, Kulkarni SR, Tan G, Baranasic D, Arenillas DJ, Sandelin A, Vandepoele K, Lenhard B, Ballester B, Wasserman WW, Parcy F, Mathelier A (2018). "JASPAR 2018: update of the open-access database of transcription factor binding profiles and its web framework." *Nucleic Acids Research*, **46**, D260-D266.

#### See Also

```
compare_motifs()
```

# **Examples**

```
## Not run:
library(MotifDb)
motifs <- convert_motifs(MotifDb[1:100])
scores <- make_DBscores(motifs, method = "PCC")
compare_motifs(motifs, 1:100, db.scores = scores)
## End(Not run)</pre>
```

merge\_motifs

Merge motifs.

# **Description**

Aligns the motifs using compare\_motifs(), then averages the motif PPMs. Currently the multifreq slot, if filled in any of the motifs, will be dropped. Only 0-order background probabilities will be kept. Motifs are merged one at a time, starting with the first entry in the list.

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#### Usage

```
merge_motifs(motifs, method = "ALLR", use.type = "PPM", min.overlap = 6,
  min.mean.ic = 0.25, tryRC = TRUE, relative_entropy = FALSE,
  normalise.scores = FALSE, min.position.ic = 0, score.strat = "sum",
  new.name = NULL)
```

# **Arguments**

motifs See convert\_motifs() for acceptable motif formats.

method character(1) One of PCC, EUCL, SW, KL, ALLR, BHAT, HELL, SEUCL,

MAN, ALLR LL, WEUCL, WPCC. See details.

use.type character(1) One of 'PPM' and 'ICM'. The latter allows for taking into ac-

count the background frequencies if relative\_entropy = TRUE. Note that 'ICM'

is not allowed when method =  $c("ALLR", "ALLR_LL")$ .

min.overlap numeric(1) Minimum overlap required when aligning the motifs. Setting this

to a number higher then the width of the motifs will not allow any overhangs. Can also be a number between 0 and 1, representing the minimum fraction that

the motifs must overlap.

min.mean.ic numeric(1) Minimum mean information content between the two motifs for

an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="average\_ic">average\_ic</a>() to filter out low IC motifs to get around this if you want to avoid

getting NAs in your output.

tryRC logical(1) Try the reverse complement of the motifs as well, report the best

score.

relative\_entropy

 $logical (1)\ Change\ the\ ICM\ calculation\ affecting\ min.\ position.\ ic\ and\ min.\ mean.\ ic.$ 

See convert\_type().

normalise.scores

logical(1) Favour alignments which leave fewer unaligned positions, as well as alignments between motifs of similar length. Similarity scores are multiplied by the ratio of aligned positions to the total number of positions in the larger

motif, and the inverse for distance scores.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help

punish scores resulting from only a fraction of an alignment.

score.strat character(1) How to handle column scores calculated from motif alignments.

"sum": add up all scores. "a.mean": take the arithmetic mean. "g.mean": take the geometric mean. "median": take the median. "wa.mean", "wg.mean": weighted arithmetic/geometric mean. "fzt": Fisher Z-transform. Weights are the

total information content shared between aligned columns.

new.name character(1), NULL Instead of collapsing existing names (if NULL), assign a

new one manually for the merged motif.

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#### **Details**

See compare\_motifs() for more info on comparison parameters.

If using a comparison metric where 0s are not allowed (KL, ALLR, ALLR\_LL, IS), then pseudocounts will be added internally. These pseudocounts are only used for comparison and alignment, and are not used in the final merging step.

Note: score.strat = "a.mean" is NOT recommended, as merge\_motifs() will not discriminate between two alignments with equal mean scores, even if one alignment is longer than the other.

#### Value

A single motif object. See convert\_motifs() for available formats.

## Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
compare_motifs()
```

#### **Examples**

```
## Not run:
library(MotifDb)
merged.motif <- merge_motifs(MotifDb[1:5])
## End(Not run)

m1 <- create_motif("TTAAACCCC", name = "1")
m2 <- create_motif("AACCC", name = "2")
m3 <- create_motif("AACCCGG", name = "3")
view_motifs(merge_motifs(c(m1, m2, m3)))</pre>
```

merge\_similar

Identify and merge similar motifs within a collection of motifs (or simply cluster motifs).

# Description

Given a list of motifs, merge\_similar() will identify similar motifs with compare\_motifs(), and merge similar ones with merge\_motifs().

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### Usage

```
merge_similar(motifs, threshold = 0.95, threshold.type = "score.abs",
  method = "PCC", use.type = "PPM", min.overlap = 6, min.mean.ic = 0,
  tryRC = TRUE, relative_entropy = FALSE, normalise.scores = FALSE,
  min.position.ic = 0, score.strat.compare = "a.mean",
  score.strat.merge = "sum", nthreads = 1, return.clusters = FALSE)
```

### **Arguments**

motifs See convert\_motifs() for acceptable motif formats.

threshold numeric(1) The minimum (for similarity metrics) or maximum (for distance

metrics) threshold score for merging.

threshold.type character(1) Type of score used for thresholding. Currently unused.

method character(1) One of PCC, EUCL, SW, KL, BHAT, HELL, SEUCL, MAN,

WEUCL, WPCC. See compare\_motifs(). (The ALLR and ALLR\_LL meth-

ods cannot be used for distance matrix construction.)

use.type character(1) One of 'PPM' and 'ICM'. The latter allows for taking into ac-

count the background frequencies if relative\_entropy = TRUE. Note that 'ICM'

is not allowed when method = c("ALLR", "ALLR\_LL").

min.overlap numeric(1) Minimum overlap required when aligning the motifs. Setting this

to a number higher then the width of the motifs will not allow any overhangs. Can also be a number between 0 and 1, representing the minimum fraction that

the motifs must overlap.

min.mean.ic numeric(1) Minimum mean information content between the two motifs for

an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="https://example.com/articles/ar

getting NAs in your output.

tryRC logical(1) Try the reverse complement of the motifs as well, report the best

score.

relative\_entropy

logical(1) Change the ICM calculation affecting min.position.ic and min.mean.ic.

See convert\_type().

normalise.scores

logical(1) Favour alignments which leave fewer unaligned positions, as well as alignments between motifs of similar length. Similarity scores are multiplied by the ratio of aligned positions to the total number of positions in the larger

motif, and the inverse for distance scores.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help punish scores resulting from only a fraction of an alignment.

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#### **Details**

See compare\_motifs() for more info on comparison parameters, and merge\_motifs() for more info on motif merging.

### Value

See convert\_motifs() for available output formats.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
compare_motifs(), merge_motifs()
```

# **Examples**

```
## Not run:
library(MotifDb)
motifs <- filter_motifs(MotifDb, family = "bHLH")[1:50]
length(motifs)
motifs <- merge_similar(motifs)
length(motifs)
## End(Not run)</pre>
```

motif\_peaks

Look for overrepresented motif position peaks in a set of sequences.

### **Description**

Using the motif position data from scan\_sequences() (or elsewhere), test whether certain positions in the sequences have significantly higher motif density.

motif\_peaks 37

# Usage

```
motif_peaks(hits, seq.length, seq.count, bandwidth, max.p = 1e-06,
   peak.width = 3, nrand = 100, plot = TRUE, BP = FALSE)
```

#### **Arguments**

hits	numeric A vector of sequence positions indicating motif sites.
seq.length	numeric(1) Length of sequences. Only one number is allowed, as all sequences must be of identical length. If missing, then the largest number from hits is used.
seq.count	numeric(1) Number of sequences with motif sites. If missing, then the number of unique values in hits is used.
bandwidth	numeric(1) Peak smoothing parameter. Smaller numbers will result in skinnier peaks, larger numbers will result in wider peaks. Leaving this empty will cause motif_peaks() to generate one by itself (see 'details').
max.p	numeric(1) Maximum P-value allowed for finding significant motif site peaks.
peak.width	numeric(1) Minimum peak width. A peak is defined as as the highest point within the value set by peak.width.
nrand	numeric(1) Number of random permutations for generating a null distribution. In order to calculate P-values, a set of random motif site positions are generated nrand times.
plot	logical(1) Will create a ggplot2 object displaying motif peaks.
BP	logical(1) Allows for the use of <b>BiocParallel</b> within motif_peaks(). See BiocParallel::register() to change the default backend. Setting BP = TRUE is only recommended for exceptionally large jobs. Keep in mind that this function will not attempt to limit its memory usage.

## Details

Kernel smoothing is used to calculate motif position density. The implementation for this process is based on code from the **KernSmooth** R package (Wand 2015). These density estimates are used to determine peak locations and heights. To calculate the P-values of these peaks, a null distribution is calculated from peak heights of randomly generated motif positions.

If the bandwidth option is not supplied, then the following code is used (from **KernSmooth**):

# Value

A DataFrame with peak positions and P-values. If plot = TRUE, then a list is returned with the DataFrame as the first item and the ggplot2 object as the second item.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### References

Wand M (2015). *KernSmooth: Functions for Kernel Smoothing Supporting Wand and Jones* (1995). R package version 2.23-15, <URL: https://CRAN.R-project.org/package=KernSmooth>.

#### See Also

```
scan_sequences()
```

### **Examples**

```
data(ArabidopsisMotif)
data(ArabidopsisPromoters)
if (R.Version()$arch != "i386") {
hits <- scan_sequences(ArabidopsisMotif, ArabidopsisPromoters, RC = FALSE)
res <- motif_peaks(as.vector(hits$start), 1000, 50)
# View plot:
res$Plot

# The raw plot data can be found in:
res$Plot$data
}</pre>
```

motif\_pvalue

*Motif P-value and scoring utility* 

## **Description**

For calculating P-values and logodds scores from P-values for any number of motifs.

# Usage

```
motif_pvalue(motifs, score, pvalue, bkg.probs, use.freq = 1, k = 8,
  nthreads = 1, rand.tries = 10, rng.seed = sample.int(10000, 1),
  allow.nonfinite = FALSE, method = c("dynamic", "exhaustive"))
```

### **Arguments**

motifs	See convert_motifs() for acceptable motif formats.
score	numeric, list Get a P-value for a motif from a logodds score. See details for an explanation of how to vectorize the calculation for method = "dynamic".
pvalue	numeric, list Get a logodds score for a motif from a P-value. See details for an explanation of how to vectorize the calculation for method = "dynamic".
bkg.probs	numeric, list A vector background probabilities. If supplying individual background probabilities for each motif, a list of such vectors. If missing, retrieves the background from the motif bkg slot. Note that this option is only used when method = "dynamic", or when method = "exhaustive" and providing a

P-value and returning a score; for the inverse, the motifs are first converted to PWMs via convert\_type(), which uses the motif bkg slot for background adjustment.

use.freq

numeric(1) By default uses the regular motif matrix; otherwise uses the corresponding multifreq matrix. Max is 3 when method = "exhaustive".

k

numeric(1) For speed, scores/P-values can be approximated after subsetting the motif every k columns when method = "exhaustive". If k is a value equal or higher to the size of input motif(s), then the calculations are exact. The default, 8, is recommended to those looking for a good tradeoff between speed and accuracy for jobs requiring repeated calculations. Note that this is ignored when method = "dynamic", as subsetting is not required.

nthreads

numeric(1) Run motif\_pvalue() in parallel with nthreads threads. nthreads
= 0 uses all available threads. Currently only applied when method = "exhaustive".

rand.tries

numeric(1) When ncol(motif) < k and method = "exhaustive", an approximation is used. This involves randomly approximating the overall motif score distribution. To increase accuracy, the distribution is approximated rand.tries times and the final scores averaged. Note that this is ignored when method = "dynamic", as subsetting is not required.

rng.seed

numeric(1) In order to allow motif\_pvalue() to perform C++ level parallelisation, it must work independently from R. This means it cannot communicate with R to get/set the R RNG state. To get around this, the RNG seed used by the C++ function can be set with rng.seed. To make sure each thread gets a different seed however, the seed is multiplied with the iteration count. For example: when working with two motifs, the second motif gets the following seed: rng.seed \* 2. The default is to pick a random number as chosen by sample(), which effectively makes motif\_pvalue() dependent on the R RNG state. Note that this is ignored when method = "dynamic", as the random subsetting is only used for method = "exhaustive".

allow.nonfinite

logical(1) If FALSE, then apply a pseudocount if non-finite values are found in the PWM. Note that if the motif has a pseudocount greater than zero and the motif is not currently of type PWM, then this parameter has no effect as the pseudocount will be applied automatically when the motif is converted to a PWM internally. Note that this option is incompatible with method = "dynamic". A message will be printed if a pseudocount is applied. To disable this, set options(pseudocount.warning=FALSE).

method

character(1) One of c("dynamic", "exhaustive"). Algorithm used for calculating P-values. The "exhaustive" method involves finding all possible motif matches at or above the specified score using a branch-and-bound algorithm, which can be computationally intensive (Hartman et al., 2013). Additionally, the computation must be repeated for each hit. The "dynamic" method calculates the distribution of possible motif scores using a much faster dynamic programming algorithm, and can be recycled for multiple scores (Grant et al., 2011). The only disadvantage is the inability to use allow.nonfinite = TRUE.

### Details

### **Regarding vectorization:**

A note regarding vectorizing the calculation when method = "dynamic" (no vectorization is possible with method = "exhaustive"): to avoid performing the P-value/score calculation repeatedly for individual motifs, provide the score/pvalue arguments as a list, with each entry corresponding to the scores/P-values to be calculated for the respective motifs provided to motifs. If you simply provide a list of repeating motifs and a single numeric vector of corresponding input scores/P-values, then motif\_pvalue() will not vectorize. See the Examples section.

### The dynamic method:

One of the algorithms available to motif\_pvalue() to calculate scores or P-values is the dynamic programming algorithm used by FIMO (Grant et al., 2011). In this method, a small range of possible scores from the possible miminum and maximum is created and the cumulative probability of each score in this distribution is incrementally calculated using the logodds scores and the background probabilities. This distribution of scores and associated P-values can be used to calculate P-values or scores for any input, any number of times. This method scales well with large motifs, and multifreq representations. The only downside is that it is incompatible with allow.nonfinite = TRUE, as this would not allow for the creation of the initial range of scores. Although described for a different purpose, the basic premise of the dynamic programming algorithm is also described in Gupta et al. (2007).

#### The exhaustive method:

Calculating P-values exhaustively for motifs can be very computationally intensive. This is due to how P-values must be calculated: for a given score, all possible sequences which score equal or higher must be found, and the probability for each of these sequences (based on background probabilities) summed. For a DNA motif of length 10, the number of possible unique sequences is  $4^10 = 1,048,576$ . Finding all possible sequences higher than a given score can be done very efficiently and quickly with a branch-and-bound algorithm, but as the motif length increases even this calculation becomes impractical. To get around this, the P-value calculation can be approximated. In order to calculate P-values for longer motifs, this function uses the approximation proposed by Hartmann et al. (2013), where the motif is subset, P-values calculated for the subsets, and finally combined for a total P-value. The smaller the size of the subsets, the faster the calculation; but also, the bigger the approximation. This can be controlled by setting k. In fact, for smaller motifs (< 13 positions) calculating exact P-values can be done individually in reasonable time by setting k = 12.

To calculate a score from a P-value, all possible scores are calculated and the (1 - pvalue) \* 100 nth percentile score returned. When k < ncol(motif), the complete set of scores is instead approximated by randomly adding up all possible scores from each subset. Note that this approximation can actually be potentially quite expensive at times and even slower than the exact version; for jobs requiring lots of repeat calculations, a bit of benchmarking beforehand can be useful to find the optimal settings.

Please note that bugs are more likely to occur when using the exhaustive method, as the algorithm contains several times more code compared to the dynamic method. Unless you have a strong need to use allow.nonfinite = TRUE then avoid using this method.

### Value

numeric, list A vector or list of vectors of scores/P-values.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Grant CE, Bailey TL, Noble WS (2011). "FIMO: scanning for occurrences of a given motif." *Bioinformatics*, **27**, 1017-1018.

Gupta S, Stamatoyannopoulos JA, Bailey TL, Noble WS (2007). "Quantifying similarity between motifs." *Genome Biology*, **8**, R24.

Hartmann H, Guthohrlein EW, Siebert M, Soding SLJ (2013). "P-value-based regulatory motif discovery using positional weight matrices." *Genome Research*, **23**, 181-194.

#### See Also

```
get_matches(), get_scores(), motif_range(), motif_score(), prob_match(), prob_match_bkg(),
score_match()
```

```
if (R.Version()$arch != "i386") {
## P-value/score calculations are performed using the PWM version of the
## motif
data(examplemotif)
## Get a minimum score based on a P-value
motif_pvalue(examplemotif, pvalue = 0.001)
## Get the probability of a particular sequence hit
motif_pvalue(examplemotif, score = 0)
## The calculations can be performed for multiple motifs
motif_pvalue(c(examplemotif, examplemotif), pvalue = c(0.001, 0.0001))
## Compare score thresholds and P-value:
scores <- motif_score(examplemotif, c(0.6, 0.7, 0.8, 0.9))</pre>
motif_pvalue(examplemotif, scores)
## Calculate the probability of getting a certain match or better:
TATATAT <- score_match(examplemotif, "TATATAT")</pre>
TATATAG <- score_match(examplemotif, "TATATAG")</pre>
motif_pvalue(examplemotif, TATATAT)
motif_pvalue(examplemotif, TATATAG)
## Get all possible matches by P-value:
get_matches(examplemotif, motif_pvalue(examplemotif, pvalue = 0.0001))
## Vectorize the calculation for multiple motifs and scores/P-values:
m <- create_motif()</pre>
motif_pvalue(c(examplemotif, m), list(1:5, 2:3))
## The non-vectorized equivalent:
```

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```
motif_pvalue(
   c(rep(list(examplemotif), 5), rep(list(m), 2)), c(1:5, 2:3)
)
}
```

motif\_rc

Get the reverse complement of a DNA or RNA motif.

# Description

For any motif, change the motif slot to it's reverse complement. If the multifreq slot is filled, then it is also applied. No other slots are affected.

# Usage

```
motif_rc(motifs, ignore.alphabet = FALSE)
```

# Arguments

# Value

See convert\_motifs() for available output formats.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

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motif\_tree

Generate ggplot2 motif trees with ggtree.

### **Description**

For more powerful motif tree functions, see the **motifStack** package. The motif\_tree() function compares motifs with compare\_motifs() to create a distance matrix, which is used to generate a phylogeny. This can be plotted with ggtree::ggtree(). The purpose of this function is simply to combine the compare\_motifs() and ggtree::ggtree() steps into one. For more control over tree creation, it is recommend to do these steps separately. See the "Motif comparisons and P-values" vignette for such a workthrough. This function requires the **ape** and **ggtree** packages to be installed separately.

# Usage

```
motif_tree(motifs, layout = "circular", linecol = "family",
  labels = "none", tipsize = "none", legend = TRUE,
  branch.length = "none", db.scores, method = "EUCL", use.type = "PPM",
  min.overlap = 6, min.position.ic = 0, tryRC = TRUE, min.mean.ic = 0,
  relative_entropy = FALSE, progress = FALSE, nthreads = 1,
  score.strat = "a.mean", ...)
```

### **Arguments**

motifs	list, dist See convert_motifs() for available formats. Alternatively, the resulting comparison matrix from compare_motifs() (run as.dist(results) beforehand; if the comparison was performed with a similarity metric, make sure to convert to distances first).
layout	<pre>character(1) One of c('rectangular', 'slanted', 'fan', 'circular',</pre>
linecol	character(1) universalmotif slot to use to colour lines (e.g. 'family'). Not available for dist input (see examples for how to add it manually). See ggtree::ggtree().
labels	character(1) universalmotif slot to use to label tips (e.g. 'name'). For dist input, only 'name' is available. See ggtree::ggtree().
tipsize	character(1) universalmotif slot to use to control tip size (e.g. 'icscore'). Not available for dist input (see examples for how to add it manually). See ggtree::ggtree().
legend	logical(1) Show legend for line colour and tip size. See ggtree::ggtree().
branch.length	character(1) If 'none', draw a cladogram. See ggtree::ggtree().
db.scores	data.frame See compare_motifs().
method	character(1) One of PCC, EUCL, SW, KL, ALLR, BHAT, HELL, SEUCL, MAN, ALLR_LL, WEUCL, WPCC. See details.
use.type	character(1)c('PPM', 'ICM'). The latter allows for taking into account the background freative_entropy = $TRUE'$ ). See compare_motifs().

44 motif\_tree

min.overlap

numeric(1) Minimum overlap required when aligning the motifs. Setting this to a number higher then the width of the motifs will not allow any overhangs. Can also be a number between 0 and 1, representing the minimum fraction that the motifs must overlap.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help punish scores resulting from only a fraction of an alignment.

tryRC

logical(1) Try the reverse complement of the motifs as well, report the best score.

min.mean.ic

numeric(1) Minimum mean information content between the two motifs for an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="average\_ic()">average\_ic()</a> to filter out low IC motifs to get around this if you want to avoid getting NAs in your output.

relative\_entropy

logical(1) Change the ICM calculation affecting min.position.ic and min.mean.ic.

See convert\_type().

progress logical(1) Show message regarding current step.

nthreads numeric(1) Run compare\_motifs() in parallel with nthreads threads. nthreads

= 0 uses all available threads.

score.strat character(1) How to handle column scores calculated from motif alignments.

"sum": add up all scores. "a.mean": take the arithmetic mean. "g.mean": take the geometric mean. "median": take the median. "wa.mean", "wg.mean": weighted arithmetic/geometric mean. "fzt": Fisher Z-transform. Weights are the

total information content shared between aligned columns.

... **ggtree** params. See ggtree::ggtree().

#### **Details**

See compare\_motifs() for more info on comparison parameters.

# Value

ggplot object.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## References

Wickham H (2009). *ggplot2: Elegant Graphics for Data Analysis*. Springer-Verlag New York. ISBN 978-0-387-98140-6, <URL: http://ggplot2.org>.

read\_cisbp 45

Yu G, Smith D, Zhu H, Guan Y, Lam TT (2017). "ggtree: an R package for visualization and annotation of phylogenetic trees with their covariates and other associated data." *Methods in Ecology and Evolution*, **8**, 28-36. doi: 10.1111/2041-210X.12628.

### See Also

```
motifStack::motifStack(), compare_motifs(), ggtree::ggtree(), ggplot2::ggplot()
```

# **Examples**

```
jaspar <- read_jaspar(system.file("extdata", "jaspar.txt",</pre>
                                    package = "universalmotif"))
if (requireNamespace("ggtree", quietly = TRUE)) {
jaspar.tree <- motif_tree(jaspar, linecol = "none", labels = "name",</pre>
                           layout = "rectangular")
}
## Not run:
## When inputting a dist object, the linecol and tipsize options are
## not available. To add these manually:
library(MotifDb)
library(ggtree)
library(ggplot2)
motifs <- filter_motifs(MotifDb, organism = "Athaliana")[1:50]</pre>
comparison <- compare_motifs(motifs, method = "PCC", score.strat = "a.mean")</pre>
comparison <- as.dist(1 - comparison)</pre>
mot.names <- attr(comparison, "Labels")</pre>
tree <- motif_tree(comparison)</pre>
annotations <- data.frame(label = mot.names,</pre>
                            icscore = sapply(motifs, function(x) x["icscore"]),
                           family = sapply(motifs, function(x) x["family"]))
tree <- tree %<+% annotations +
          geom_tippoint(aes(size = icscore)) +
          aes(colour = family) +
          theme(legend.position = "right",
                 legend.title = element_blank())
## End(Not run)
```

read\_cisbp

Import CIS-BP motifs.

#### Description

Import CIS-BP formatted motifs. See <a href="http://cisbp.ccbr.utoronto.ca/index.php">http://cisbp.ccbr.utoronto.ca/index.php</a>. Assumed to be DNA motifs.

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### Usage

```
read_cisbp(file, skip = 0)
```

# **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

#### **Details**

CIS-BP motifs can be formatted with or without additional header metadata. Motifs without any header start at instances of the word "Pos", whereas motifs with a header start at instances of the word "TF".

### Value

list universalmotif objects.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Weirauch MT, Yang A, Albu M, Cote AG, Montenegro-Montero A, Drewe P, Najafabadi HS, Lambert SA, Mann I, Cook K, Zheng H, Goity A, van Bakel H, Lozano JC, Galli M, Lewsey MG, Huang E, Mukherjee T, Chen X, Reece-Hoyes JS, Govindarajan S, Shaulsky G, Walhout AJ, Bouget FY, Ratsch G, Larrondo LF, Ecker JR, Hughes TR (2014). "Determination and inference of eukaryotic transcription factor sequence specificity." *Cell*, **158**, 1431-1443.

#### See Also

```
Other read_motifs: read_homer(), read_jaspar(), read_matrix(), read_meme(), read_motifs(), read_transfac(), read_uniprobe()
```

read\_homer 47

read\_homer

Import HOMER motifs.

### **Description**

Import HOMER formatted motifs. See <a href="http://homer.ucsd.edu/homer/motif/">http://homer.ucsd.edu/homer/motif/</a>. Assumed to be DNA motifs. Note that HOMER motifs come with a pre-determined logodds threshold; if you wish to re-create HOMER's motif scanning, then use it in <a href="mailto:scan\_sequences">scan\_sequences</a>() (see examples).

# Usage

```
read_homer(file, skip = 0)
```

#### **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

#### Value

list universalmotif objects.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### References

Heinz S, Benner C, Spann N, Bertolino E, Lin YC, Laslo P, Cheng JX, Murre C, Singh H, Glass CK (2010). "Simple combinations of lineage-determining transcription factors prime cis-regulatory elements required for macrophage and B cell identities." *Molecular Cell*, **38**, 576-589.

#### See Also

```
Other read_motifs: read_cisbp(), read_jaspar(), read_matrix(), read_meme(), read_motifs(), read_transfac(), read_uniprobe()
```

48 read\_jaspar

read\_jaspar

Import JASPAR motifs.

### Description

Import JASPAR formatted motifs. See <a href="http://jaspar.genereg.net/">http://jaspar.genereg.net/</a>. Can be either DNA, RNA, or AA motifs.

## Usage

```
read_jaspar(file, skip = 0)
```

# **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

### Value

list universalmotif objects.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### References

Khan A, Fornes O, Stigliani A, Gheorghe M, Castro-Mondragon JA, van der Lee R, Bessy A, Cheneby J, Kulkarni SR, Tan G, Baranasic D, Arenillas DJ, Sandelin A, Vandepoele K, Lenhard B, Ballester B, Wasserman WW, Parcy F, Mathelier A (2018). "JASPAR 2018: update of the open-access database of transcription factor binding profiles and its web framework." *Nucleic Acids Research*, **46**, D260-D266.

# See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_matrix(), read_meme(), read_motifs(), read_transfac(), read_uniprobe()
```

read\_matrix 49

|--|

# **Description**

Import simply formatted motifs.

# Usage

```
read_matrix(file, skip = 0, type, positions = "columns",
   alphabet = "DNA", sep = "", headers = TRUE, rownames = FALSE,
   comment = NULL)
```

# Arguments

file	character(1) File name.
skip	numeric(1) If not zero, will skip however many desired lines in the file before starting to read.
type	character(1) One of c('PCM', 'PPM', 'PWM', 'ICM'). If missing will try and guess which one.
positions	character(1) One of c('columns', 'rows'). Partial matching allowed. Indicate whether each position within a motif is represented as a row or a column in the file.
alphabet	character(1) One of c('DNA', 'RNA', 'AA'), or a string of letters.
sep	character(1) Indicates how individual motifs are separated. Set as NULL if there are no seperating lines between motifs (the default is to assume a blank line).
headers	logical(1), character(1) Indicating if and how to read names.
rownames	logical(1) Are there alphabet letters present as rownames?
comment	NULL, character(1) Character denoting lines to be considered comments.

## Value

list universalmotif objects.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

# See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_jaspar(), read_meme(), read_motifs(), read_transfac(), read_uniprobe()
```

50 read\_meme

#### **Examples**

```
hocomoco <- system.file("extdata", "hocomoco.txt", package = "universalmotif")
hocomoco <- read_matrix(hocomoco, headers = ">", positions = "rows")
```

read\_meme

Import MEME motifs.

### **Description**

Import MEME formatted motifs, as well as original motif sequences. See <a href="http://meme-suite.org/doc/meme-format.html">http://meme-suite.org/doc/meme-format.html</a>. Both 'full' and 'minimal' formats are supported. DREME and STREME motifs can also be imported, but note that readsites and readsites.meta arguments do nothing.

### Usage

```
read_meme(file, skip = 0, readsites = FALSE, readsites.meta = FALSE,
  readsites.meta.tidy = FALSE)
```

#### **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

readsites logical(1) If TRUE, the motif sites will be read as well.

readsites.meta logical(1) If readsites = TRUE, then additionally read site positions and P-

values.

readsites.meta.tidy

logical(1) If readsites.meta = TRUE, merge the position site information for

all motifs into a single tidy data. frame.

# **Details**

Please note that the typical number precision limit in R is around 1e-308. This means that motif P-values in MEME files below this limit are rounded automatically to 0. To get around this, the E-value is also stored as a string in the extrainfo slot. If you require a numeric value for analysis, use the log\_string\_pval() function to get the log of the string-formatted p-value.

### Value

list universalmotif objects. If readsites = TRUE, a list comprising of a sub-list of motif objects and a sub-list of motif sites will be returned. If readsites.meta = TRUE, then two additional list items will be present, one containing site positions and P-values, and another containing combined sequence p-values. If readsites.meta.tidy = TRUE, an additional list entry named sites.meta.tidy will be added containing a data.frame.

read\_motifs 51

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Bailey TL, Boden M, Buske FA, Frith M, Grant CE, Clementi L, Ren J, Li WW, Noble WS (2009). "MEME SUITE: tools for motif discovery and searching." *Nucleic Acids Research*, **37**, W202-W208.

#### See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_jaspar(), read_matrix(), read_motifs(), read_transfac(), read_uniprobe()
```

### **Examples**

read\_motifs

Import universalmotif formatted motifs.

# Description

Import motifs created from write\_motifs(). For optimal storage of universalmotif class motifs, consider using saveRDS() and readRDS(). Currently the universalmotif format is YAML-based, but this is subject to change.

### Usage

```
read_motifs(file, skip = 0, progress = FALSE, BP = FALSE)
```

## **Arguments**

file	character(1) File name.
skip	$\label{eq:numeric} \mbox{numeric(1) If not zero, will skip however many desired lines in the file before starting to read.}$
progress	logical(1) Show progress.
ВР	logical(1) Allows for the use of <b>BiocParallel</b> within read_motifs(). See BiocParallel::register() to change the default backend.

52 read\_transfac

### Value

list universalmotif objects.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_jaspar(), read_matrix(), read_meme(), read_transfac(), read_uniprobe()
```

read\_transfac

Import TRANSFAC motifs.

### **Description**

Import TRANSFAC formatted motifs. Assumed to be DNA motifs, type PCM. See system.file("extdata", "transfac.txt", pacakge="universalmotif") for an example motif.

### Usage

```
read_transfac(file, skip = 0)
```

### **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

### **Details**

A few TRANSFAC tags are recognized, including AC, ID, NA, HC and OS. HC will be set to the family slot and OS to the organism slot. If AC, ID and NA are present, then AC will be set as the motif name and NA as the alternate name. If AC is absent, then ID is set as the name. If ID is also absent, then NA is set as the motif name.

# Value

list universalmotif objects.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

read\_uniprobe 53

### References

Wingender E, Dietze P, Karas H, Knuppel R (1996). "TRANSFAC: A Database on Transcription Factors and Their DNA Binding Sites." *Nucleic Acids Research*, **24**, 238-241.

# See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_jaspar(), read_matrix(), read_meme(), read_motifs(), read_uniprobe()
```

# Examples

read\_uniprobe

Import UNIPROBE motifs.

# **Description**

Import UNIPROBE formatted motifs. Assumed DNA.

# Usage

```
read_uniprobe(file, skip = 0)
```

### **Arguments**

file character(1) File name.

skip numeric(1) If not zero, will skip however many desired lines in the file before

starting to read.

# Value

list universalmotif objects.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### References

Hume MA, Barrera LA, Gisselbrecht SS, Bulyk ML (2015). "UniPROBE, update 2015: new tools and content for the online database of protein-binding microarray data on protein-DNA interactions." *Nucleic Acids Research*, **43**, D117-D122.

54 run\_meme

#### See Also

```
Other read_motifs: read_cisbp(), read_homer(), read_jaspar(), read_matrix(), read_meme(), read_motifs(), read_transfac()
```

### **Examples**

reexports

Objects exported from other packages

# **Description**

These objects are imported from other packages. Follow the links below to see their documentation.

**BiocGenerics** as.data.frame, cbind, colnames, ncol, normalize, nrow, rownames, subset **MatrixGenerics** colMeans, colSums, rowMeans, rowSums

run\_meme

Run MEME from within R.

### **Description**

De novo motif discovery via MEME. For a detailed description of the command, see <a href="http://meme-suite.org/doc/meme.html">http://meme-suite.org/doc/meme.html</a>. For a brief description of the command parameters, call run\_meme() without any arguments. Parameters in run\_meme() which are directly taken from the MEME program are tagged with [MEME]. This function requires that the **processx** package be installed separately.

### Usage

```
run_meme(target.sequences, output = NULL, overwrite.dir = FALSE,
  control.sequences = NULL, weights = NULL, text = FALSE, brief = 1000,
  objfun = "classic", test = NULL, use_llr = FALSE, shuf = 2,
  hsfrac = NULL, cefrac = NULL, searchsize = NULL, norand = FALSE,
  csites = 1000, seed = 0, alph = NULL, revcomp = FALSE, pal = FALSE,
  mod = "zoops", nmotifs = 3, evt = NULL, nsites = NULL,
  minsites = NULL, maxsites = NULL, wnsites = 0.8, w = NULL,
  minw = 8, maxw = 50, allw = NULL, nomatrim = FALSE, wg = 11,
  ws = 1, noendgaps = FALSE, bfile = NULL, markov_order = 0,
  psp = NULL, maxiter = 50, distance = 0.001, prior = NULL, b = NULL,
```

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```
plib = NULL, spfuzz = NULL, spmap = NULL, cons = NULL, p = NULL,
maxsize = NULL, maxtime = NULL, wd = getwd(), logfile = paste0(wd,
"/memerun.log"), readsites = TRUE, echo = FALSE, verbose = 1,
timeout = Inf, bin = getOption("meme.bin"))
```

### **Arguments**

minw

numeric(1) [MEME]

```
target.sequences
                XStringSet List of sequences to get motifs from.
output
                character(1) Name of the output folder. If NULL, MEME output will be
overwrite.dir
                logical(1) If output is set but already exists, allow over-writing.
control.sequences
                XStringSet List of negative sequences. Only used if objfun = c("de", "se").
weights
                numeric Vector of numbers between 0 and 1, representing sequence weights.
                logical(1) [MEME]
text
brief
                numeric(1) [MEME]
objfun
                character(1) [MEME]
test
                character(1) [MEME]
use_llr
                logical(1) [MEME]
shuf
                numeric(1) [MEME]
hsfrac
                numeric(1) [MEME]
cefrac
                numeric(1) [MEME]
                numeric(1) [MEME]
searchsize
norand
                logical(1) [MEME]
                numeric(1) [MEME]
csites
seed
                numeric(1) [MEME]
alph
                character(1) [MEME] Note: custom alphabet definition files can be created
                using meme_alph().
                logical(1) [MEME]
revcomp
pal
                logical(1) [MEME]
mod
                character(1) [MEME]
nmotifs
                numeric(1) [MEME]
evt
                numeric(1) [MEME]
nsites
                numeric(1) [MEME]
minsites
                numeric(1) [MEME]
maxsites
                numeric(1) [MEME]
                numeric(1) [MEME]
wnsites
                numeric(1) [MEME]
```

run\_meme

maxw	numeric(1) [MEME]
allw	numeric(1) [MEME]
nomatrim	logical(1) [MEME]
wg	numeric(1) [MEME]
WS	numeric(1) [MEME]
noendgaps	logical(1) [MEME]
bfile	character(1) [MEME]
markov_order	numeric(1) [MEME]
psp	character(1) [MEME]
maxiter	numeric(1) [MEME]
distance	numeric(1) [MEME]
prior	character(1) [MEME]
b	numeric(1) [MEME]
plib	character(1) [MEME]
spfuzz	numeric(1) [MEME]
spmap	character(1) [MEME]
cons	character(1) [MEME]
р	numeric(1) [MEME]
maxsize	numeric(1) [MEME]
maxtime	numeric(1) [MEME]
wd	character(1) Working directory to run MEME in.
logfile	character(1) File to dump MEME stderr. If NULL, no logs will be saved.
readsites	logical(1) Read sites from MEME output (from read_meme()).
echo	logical(1) Dump MEME output to console.
verbose	<pre>numeric(1) Set verbose = 0 to quiet run_meme().</pre>
	1 (4) (4) (4) (4) (4)

numeric(1) Stop MEME program past timeout (seconds). See processx::run().

character(1) Location of MEME binary. Alternatively, set this via options (meme.bin

# Value

timeout

bin

list The output file is read with read\_meme().

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

= '/path/to/meme/bin').

### References

Bailey TL, Elkan C (1994). "Fitting a mixture model by expectation maximization to discover motifs in biopolymers." *Proceedings of the Second International Conference on Intelligent Systems for Molecular Biology*, **2**, 28-36.

sample\_sites 57

### See Also

```
read_meme(), create_sequences(), shuffle_sequences(), processx::run()
```

# **Examples**

```
## Not run:
## To check that you are properly linking to the binary:
run_meme()
## End(Not run)
```

sample\_sites

Generate binding sites from a motif.

# Description

Given probabilities for a sequence as represented by a motif, generate random sequences with the same length as the motif.

# Usage

```
sample_sites(motif, n = 100, use.freq = 1)
```

# Arguments

motif See convert\_motifs() for acceptable formats.

n numeric(1) Number of sites to generate.

use.freq numeric(1) If one, use regular motif matrix. Otherwise, use respective multifreq

matrix.

# Value

```
XStringSet object.
```

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### See Also

```
create_sequences(), create_motif(), add_multifreq()
```

```
motif <- create_motif()
sites <- sample_sites(motif)</pre>
```

58 scan\_sequences

scan_sequences	Scan sequences for matches to input motifs.	

# **Description**

For sequences of any alphabet, scan them using the PWM matrices of a set of input motifs.

# Usage

```
scan_sequences(motifs, sequences, threshold = 1e-04,
   threshold.type = c("pvalue", "qvalue", "logodds", "logodds.abs"),
   RC = FALSE, use.freq = 1, verbose = 0, nthreads = 1,
   motif_pvalue.k = 8, use.gaps = TRUE, allow.nonfinite = FALSE,
   warn.NA = TRUE, calc.pvals = TRUE, return.granges = FALSE,
   no.overlaps = FALSE, no.overlaps.by.strand = FALSE,
   no.overlaps.strat = c("score", "order"), respect.strand = FALSE,
   motif_pvalue.method = c("dynamic", "exhaustive"),
   calc.qvals = calc.pvals, calc.qvals.method = c("fdr", "BH",
   "bonferroni"))
```

## **Arguments**

motifs	See convert_motifs() for acceptable motif formats.
sequences	XStringSet Sequences to scan. Alphabet should match motif.
threshold	numeric(1) See details.
threshold.type	<pre>character(1) One of c('pvalue', 'qvalue', 'logodds', 'logodds.abs').</pre> <pre>See details.</pre>
RC	logical(1) If TRUE, check reverse complement of the input sequences. Only available for DNA/RNA.
use.freq	numeric(1) The default, 1, uses the motif matrix (from the motif['motif'] slot) to search for sequences. If a higher number is used, then the matching k-let matrix from the motif['multifreq'] slot is used. See add_multifreq().
verbose	numeric(1) Describe progress, from none (0) to verbose (3).
nthreads	numeric(1) Run scan_sequences() in parallel with nthreads threads. nthreads = 0 uses all available threads. Note that no speed up will occur for jobs with only a single motif and sequence.
<pre>motif_pvalue.k</pre>	<pre>numeric(1) Control motif_pvalue() approximation. See motif_pvalue(). Only used if motif_pvalue.method = "exhaustive".</pre>
use.gaps	logical(1) Set this to FALSE to ignore motif gaps, if present.
allow.nonfinite	
	logical(1) If FALSE, then apply a pseudocount if non-finite values are found in the PWM. Note that if the motif has a pseudocount greater than zero and the motif is not currently of type PWM, then this parameter has no effect as the pseudocount will be applied automatically when the motif is converted to a PWM

59 scan\_sequences

> internally. This value is set to FALSE by default in order to stay consistent with pre-version 1.8.0 behaviour. Also note that this parameter is not compatible with motif\_pvalue.method = "dynamic". A message will be printed if a pseudocount is applied. To disable this, set options(pseudocount.warning=FALSE).

warn.NA

logical(1) Whether to warn about the presence of non-standard letters in the input sequence, such as those in masked sequences.

calc.pvals

logical(1) Calculate P-values for each hit. This is a convenience option which simply gives motif\_pvalue() the input motifs and the scores of each hit. Be careful about setting this to TRUE if you anticipate getting thousands of hits and are using motif\_pvalue.method = "exhaustive": expect to wait a few seconds or minutes for the calculations to finish. Increasing the nthreads value can help greatly here. See Details for more information on P-value calculation. If motif\_pvalue.method = "dynamic", then this is usually not an issue.

return.granges logical(1) Return the results as a GRanges object. Requires the GenomicRanges package to be installed.

no.overlaps

logical(1) Remove overlapping hits from the same motifs. Overlapping hits from different motifs are preserved. Please note that the current implementation of this feature can add significantly to the run time for large inputs.

no.overlaps.by.strand

logical(1) Whether to discard overlapping hits from the opposite strand (TRUE), or to only discard overlapping hits on the same strand (FALSE).

no.overlaps.strat

character(1) One of c("score", "order"). The former option keeps the highest scoring overlapping hit (and the first of these within ties), and the latter simply keeps the first overlapping hit.

respect.strand logical(1) If motifs are DNA/RNA, then setting this option to TRUE will make scan\_sequences() only scan the strands of the input sequences as indicated in the motif strand slot.

motif\_pvalue.method

character(1) One of c("dynamic", "exhaustive"). Algorithm used for calculating P-values. The "exhaustive" method involves finding all possible motif matches at or above the specified score using a branch-and-bound algorithm, which can be computationally intensive (Hartman et al., 2013). Additionally, the computation must be repeated for each hit. The "dynamic" method calculates the distribution of possible motif scores using a much faster dynamic programming algorithm, and can be recycled for multiple scores (Grant et al., 2011). The only disadvantage is the inability to use allow.nonfinite = TRUE. See motif\_pvalue() for details.

calc.qvals

logical(1) Whether to also calculate adjusted P-values. Only valid if calc.pvals = TRUE.

calc.gvals.method

character(1) One of c("fdr", "BH", "bonferroni"). The method for calculating adjusted P-values. These are described in depth in the Sequence Searches vignette. Also see Noble (2009).

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#### **Details**

#### Logodds scoring:

Similar to Biostrings::matchPWM(), the scanning method uses logodds scoring. (To see the scoring matrix for any motif, simply run convert\_type(motif, "PWM"). For a multifreq scoring matrix: apply(motif["multifreq"][["2"]], 2, ppm\_to\_pwm)). In order to score a sequence, at each position within a sequence of length equal to the length of the motif, the scores for each base are summed. If the score sum is above the desired threshold, it is kept.

#### Thresholds:

If threshold.type = 'logodds', then the threshold value is multiplied by the maximum possible motif scores. To calculate the maximum possible scores a motif (of type PWM) manually, run motif\_score(motif, 1). If threshold.type = 'pvalue', then threshold logodds scores are generated using motif\_pvalue(). Finally, if threshold.type = 'logodds.abs', then the exact values provided will be used as thresholds. Finally, if threshold.type = 'qvalue', then the threshold is calculated as if threshold.type = 'pvalue' and the final set of hits are filtered based on their calculated Q-value. (Note: this means that the thresh.score column will be incorrect!) This is done since most Q-values cannot be calculated prior to scanning. If you are running a very large job, it may be wise to use a P-value threshold followed by manually filtering by Q-value; this will avoid the scanning have to parse the larger number of hits from the internally-lowered threshold.

#### Non-standard letters:

Non-standard letters (such as "N", "+", "-", ".", etc in DNAString objects) will be safely ignored, resulting only in a warning and a very minor performance cost. This can used to scan masked sequences. See Biostrings::mask() for masking sequences (generating MaskedXString objects), and Biostrings::injectHardMask() to recover masked XStringSet objects for use with scan\_sequences(). There is also a provided wrapper function which performs both steps: mask\_seqs().

#### Value

DataFrame, GRanges with each row representing one hit. If the input sequences are DNAStringSet or RNAStringSet, then an additional column with the strand is included. Function args are stored in the metadata slot. If return.granges = TRUE then a GRanges object is returned.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Grant CE, Bailey TL, Noble WS (2011). "FIMO: scanning for occurrences of a given motif." *Bioinformatics*, **27**, 1017-1018.

Hartmann H, Guthohrlein EW, Siebert M, Soding SLJ (2013). "P-value-based regulatory motif discovery using positional weight matrices." *Genome Research*, **23**, 181-194.

Noble WS (2009). "How does multiple testing work?" Nature Biotechnology, 27, 1135-1137.

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### See Also

```
add_multifreq(), Biostrings::matchPWM(), enrich_motifs(), motif_pvalue()
```

#### **Examples**

```
## any alphabet can be used
## Not run:
set.seed(1)
alphabet <- paste(c(letters), collapse = "")</pre>
motif <- create_motif("hello", alphabet = alphabet)</pre>
sequences <- create_sequences(alphabet, seqnum = 1000, seqlen = 100000)</pre>
scan_sequences(motif, sequences)
## End(Not run)
## Sequence masking:
if (R.Version()$arch != "i386") {
library(Biostrings)
data(ArabidopsisMotif)
data(ArabidopsisPromoters)
seq <- mask_seqs(ArabidopsisPromoters, "AAAAA")</pre>
scan_sequences(ArabidopsisMotif, seq)
# A warning regarding the presence of non-standard letters will be given,
# but can be safely ignored in this case.
}
```

sequence\_complexity

Calculate sequence complexity.

### **Description**

Calculate sequence complexity using either the Wootton-Federhen, Trifonov, or DUST algorithms.

# Usage

```
sequence_complexity(seqs, window.size = 20,
  window.overlap = round(window.size/2), method = c("WoottonFederhen",
  "WoottonFederhenFast", "Trifonov", "TrifonovFast", "DUST"),
  trifonov.max.word.size = 7, nthreads = 1, return.granges = FALSE)
```

# Arguments

seqs XStringSet Input sequences.

window.size numeric Window size. If a number between 0 and 1 is provided, the value is

calculated as the number multiplied by the sequence length.

window.overlap numeric Overlap between windows. If a number between 0 and 1 is provided,

the value is calculated as the number multiplied by the sequence length.

method

character(1) Choose one of the available methods for calculating sequence complexity. See details.

trifonov.max.word.size

numeric(1) The maximum word size within each window used to calculate complexity using method = c("Trifonov", "TrifonovFast"). In other words, the Trifonov method involves counting the number of possible different subwords in a window at different sizes up to the values provided by this option. It also involves calculating the product of ever increasing sequences of numbers and so in order to reduce the computations involed this can be limited to a specific maximum sub-word size.

nthreads

numeric(1) Run sequence\_complexity() in parallel with nthreads threads.

nthreads = 0 uses all available threads.

return.granges logical(1) Return the results as a GRanges object. Requires the GenomicRanges package to be installed.

#### **Details**

The Wootton-Federhen (Wootton and Federhen, 1993) and Trifonov (Trifonov, 1990) algorithms as well as their faster approximations are well described within Orlov and Potapov (2004). These algorithms score less complex sequences closer to 0, and more complex ones closer to 1. Please note that the 'fast' approximation versions of the two methods are not actually faster within sequence\_complexity(), and so speed should not be a major consideration when choosing which method to use within the universalmotif package. The DUST algorithm implementation is described in Morgulis et al. (2006). In this case, less complex sequences score higher, and more complex ones closer to 0.

Briefly, the Wootton-Federhen complexity score is a reflection of the numbers of each unique letter found in the window (e.g. for DNA, the more of all four letters can be found in the window the higher the score). An increasing Trifonov score is a relection of the numbers of increasingly larger k-mers (e.g. the count of possible 1-mers, 2-mers, 3-mers, ..., until trifonov.max.word.size). Finally, the DUST score approaches 0 as the count of unique 3-mers increases. (See the final section in the examples to see how different types of sequence compositions affect the methods.)

Please note that the authors of the different methods recommend various window sizes and complexity thresholds. The authors of DUST for example, suggest using a window size of 64 and a threshold of 2 for low complexity. Wootton and Federhen suggest a window size of 40, though show that 10 and 20 can be appropriate as well (for amino acid sequences). Keep in mind however that these algorithms were implemented at a time when computers were much slower; perhaps the authors would suggest different window sizes today. One thing to note is that the Wootton-Federhen algorithm has a hard limit due to the need to caculate the product from 1:window.size. This can end up calculating values which are greater than what a double can hold (e.g. try prod(1:500)). Its approximation does not suffer from this though, as it skips calculating the product.

In terms of speed, the Wootton-Federhen algorithms are fastest, with DUST being 1-3 times slower and the Trifonov algorithms being several times slower (though the exact amount depends on the max word size).

#### Value

DataFrame, GRanges with each row getting a complexity score for each window in each input sequence.

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#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Morgulis A, Gertz EM, Schaffer AA, Agarwala R (2006). "A fast and symmetric DUST implementation to mask low-complexity DNA sequences." *Journal of Computational Biology*, **13**, 1028-1040.

Orlov YL, Potapov VN (2004). "Complexity: an internet resource for analysis of DNA sequence complexity." *Nucleic Acids Research*, **32**, W628-W633.

Trifonov EN (1990). "Making sense of the human genome." In Sarma RH, Sarma MH (Eds), *Structure & Methods* Adenine Press, Albany, **1**, 69-77.

Wootton JC, Federhen S (1993). "Statistics of local complexity in amino acid sequences and sequence databases." *Computers & Chemistry*, **17**, 149-163.

#### See Also

```
calc_complexity(), count_klets(), get_bkg(), mask_ranges(), mask_seqs()
```

```
## Feel free to play around with different toy sequences to get a feel for
## how the different methods perform
library(Biostrings)
test.seq <- DNAStringSet(c("AAAAAAAAAA", "ATGACTGATGC"))</pre>
sequence_complexity(test.seq, method = "WoottonFederhen")
sequence_complexity(test.seq, method = "WoottonFederhenFast")
sequence_complexity(test.seq, method = "Trifonov")
sequence_complexity(test.seq, method = "TrifonovFast")
sequence_complexity(test.seq, method = "DUST")
## You could also use this in conjuction with mask_ranges() to hide
## low complexity regions from scanning, de novo motif discovery, etc
if (requireNamespace("GenomicRanges", quiet = TRUE)) {
data(ArabidopsisPromoters)
# Calculate complexity in 20 bp windows, sliding every 1 bp
to.mask <- sequence_complexity(ArabidopsisPromoters, method = "DUST",</pre>
 window.size = 20, window.overlap = 19, return.granges = TRUE)
# Get the ranges with a complexity score greater than 3.5
to.mask <- to.mask[to.mask$complexity > 3.5]
# See what the low complexity regions look like
ArabidopsisPromoters[IRanges::reduce(to.mask)]
# Mask them with the default '-' character:
mask_ranges(ArabidopsisPromoters, to.mask)
```

```
}
## To demonstrate how the methods work, consider:
## (These examples use the calc_complexity() utility which utilizes
## the same algorithms and works on character vectors, but lacks
## the ability to use sliding windows.)
a <- "ACGT"
# For Wootton-Federhen, it can be easily shown it is only dependent
# on the counts of individual letters (though do note that the
# original paper discusses this method in the context of amino acid
calc_complexity("AAACCCGGGTTT", alph = a) # 0.7707
calc_complexity("AACCGGTTACGT", alph = a) # 0.7707
calc_complexity("ACGTACGTACGT", alph = a) # 0.7707
# As letters start to see drops in counts, the scores go down too:
calc_complexity("AAAACCCCGGGG", alph = a) # 0.6284
calc_complexity("AAAAAACCCCCC", alph = a) # 0.4105
calc_complexity("AAAAAAAAAACC", alph = a) # 0.2518
# Trifonov on the other hand is greatly affected by the number
# of higher order combinations:
calc_complexity("AAACCCGGGTTT", c = "Trifonov", alph = a) # 0.6364
calc_complexity("AACCGGTTACGT", c = "Trifonov", alph = a) # 0.7273
# This next one may seem surprising, but it indeed scores very low.
# This is because although it has many of each individual letter,
# the number of higher order letter combinations in fact is quite
# low due to this particular repeating pattern!
calc_complexity("ACGTACGTACGT", c = "Trifonov", alph = a) # 0.01231
# By extension, this means it scores sequences with fewer
# counts of individual letters lower too.
calc_complexity("AAAACCCCGGGG", c = "Trifonov", alph = a) # 0.2386
calc_complexity("AAAAAACCCCCCC", c = "Trifonov", alph = a) # 0.0227
calc_complexity("AAAAAAAAAACC", c = "Trifonov", alph = a) # 0.0011
# As for DUST, it considers the number of 3-mers in the sequence.
# The higher the numbers of 3-mers, the lower the score.
# (0 = the max possible number of DNA 3-mers for the window size)
calc_complexity("AAACCCGGGTTT", c = "DUST", alph = a) # 0
calc_complexity("AACCGGTTACGT", c = "DUST", alph = a) # 0
calc_complexity("ACGTACGTACGT", c = "DUST", alph = a) # 0.8889
calc_complexity("AAAACCCCGGGG", c = "DUST", alph = a) # 0.333
calc_complexity("ACGACGACGACG", c = "DUST", alph = a) # 1.333
calc_complexity("AAAAAACCCCCC", c = "DUST", alph = a) # 1.333
# Similarly to Trifonov, the next one also scores as less complex
# compared to the previous one:
calc_complexity("ACACACACACAC", c = "DUST", alph = a) # 2.222
calc_complexity("AAAAAAAAAACC", c = "DUST", alph = a) # 3.111
calc_complexity("AAAAAAAAAAAC", c = "DUST", alph = a) # 4
calc_complexity("AAAAAAAAAAA", c = "DUST", alph = a) # 5
```

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```
# Just to show once more why the seemingly more complex sequences
# such as "ACACACACACAC" score as less complex than "AAAAAACCCCCC"
# for the Trifonov and DUST methods:
count_klets("ACACACACACAC", k = 3) # Only 2 possible 3-mers
count_klets("AAAAAACCCCCC", k = 3) # Now 4 possible 3-mers!
```

shuffle\_motifs

Shuffle motifs by column.

### **Description**

Given a set of motifs, shuffle the columns to create new motifs. Currently does not support keeping the 'multifreq' slot. Only the 'bkg', 'nsites', 'strand', and 'bkgsites' slots will be preserved. Uses the same shuffling methods as shuffle\_sequences(). When shuffling more than one motif, all motif columns are merged into a single pool and shuffled together, finally returning them as motifs of identical lengths as the input motifs. To instead shuffle motifs individually, call shuffle\_motifs() using lapply().

# Usage

```
shuffle_motifs(motifs, k = 2, method = "linear")
```

### **Arguments**

motifs See convert\_motifs() for acceptable formats.

k numeric(1) K-let size.

method character(1) Currently only 'linear' is accepted.

### Value

Motifs. See convert\_motifs() for available output formats.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
shuffle_sequences()
```

shuffle\_sequences

shuffle_sequences	Shuffle input sequences.
-------------------	--------------------------

# **Description**

Given a set of input sequences, shuffle the letters within those sequences with any k-let size.

# Usage

```
shuffle_sequences(sequences, k = 1, method = "euler", nthreads = 1,
    rng.seed = sample.int(10000, 1), window = FALSE, window.size = 0.1,
    window.overlap = 0.01)
```

# Arguments

sequences	XStringSet Set of sequences to shuffle. Works with any set of characters.
k	numeric(1) K-let size.
method	<pre>character(1) One of c('euler', 'markov', 'linear'). Only relevant if k &gt; 1. See details.</pre>
nthreads	numeric(1) Run shuffle_sequences() in parallel with nthreads threads. nthreads = 0 uses all available threads. Note that no speed up will occur for jobs with only a single sequence.
rng.seed	numeric(1) Set random number generator seed. Since shuffling can occur simultaneously in multiple threads using C++, it cannot communicate with the regular R random number generator state and thus requires an independent seed. Each individual sequence in an XStringSet object will be given the following seed: rng.seed * index. The default is to pick a random number as chosen by sample(), which effectively is making shuffle_sequences() dependent on the R RNG state.
window	logical(1) Shuffle sequences iteratively over windows instead of all at once.
window.size	numeric(1) Window size. Can be a fraction less than one, or an integer representing the actual window size.
window.overlap	numeric(1) Overlap between windows. Can be a fraction less than one, or an

### **Details**

### markov method:

If method = 'markov', then the Markov model is used to generate sequences which will maintain (on average) the k-let frequencies. Please note that this method is not a 'true' shuffling, and for short sequences (e.g. <100bp) this can result in slightly more dissimilar sequences versus true shuffling. See Fitch (1983) for a discussion on the topic.

integer representing the actual overlap size.

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#### euler method:

If method = 'euler', then the sequence shuffling method proposed by Altschul and Erickson (1985) is used. As opposed to the 'markov' method, this one preserves exact k-let frequencies. This is done by creating a k-let edge graph, then following a random Eulerian walk through the graph. Not all walks will use up all available letters however, so the cycle-popping algorithm proposed by Propp and Wilson (1998) is used to find a random Eulerian path. A side effect of using this method is that the starting and ending sequence letters will remain unshuffled.

### linear method:

If method = 'linear', then the input sequences are split linearly every k letters. For example, for k = 3 'ACAGATAGACCC' becomes 'ACA GAT AGA CCC'; after which these 3-lets are shuffled randomly.

### Single-letter shuffling:

Do note however, that the method parameter is only relevant for k > 1. For k = 1, a simple shuffling is performed using the shuffle function from the C++ standard library.

### Value

XStringSet The input sequences will be returned with identical names and lengths.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## References

Altschul SF, Erickson BW (1985). "Significance of Nucleotide Sequence Alignments: A Method for Random Sequence Permutation That Preserves Dinucleotide and Codon Usage." *Molecular Biology and Evolution*, **2**, 526-538.

Fitch WM (1983). "Random sequences." Journal of Molecular Biology, 163, 171-176.

Propp JG, Wilson DW (1998). "How to get a perfectly random sample from a generic markov chain and generate a random spanning tree of a directed graph." *Journal of Algorithms*, **27**, 170-217.

#### See Also

```
create_sequences(), scan_sequences(), enrich_motifs(), shuffle_motifs()
```

```
if (R.Version()$arch != "i386") {
  sequences <- create_sequences()
  sequences.shuffled <- shuffle_sequences(sequences, k = 2)
}</pre>
```

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switch\_alph

Switch between DNA and RNA alphabets.

# **Description**

Convert a motif from DNA to RNA, or RNA to DNA.

# Usage

```
switch_alph(motifs)
```

# Arguments

motifs

See convert\_motifs() for acceptable formats.

# Value

The DNA/RNA version of the motifs. See convert\_motifs() for acceptable output formats.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

### See Also

```
create_motif()
```

### **Examples**

```
DNA.motif <- create_motif()
RNA.motif <- switch_alph(DNA.motif)</pre>
```

tidy-motifs

Tidy manipulation of motifs.

# **Description**

Tidy manipulation of motifs.

# Usage

```
to_df(motifs, extrainfo = TRUE)
update_motifs(motif_df, extrainfo = TRUE, force = FALSE)
to_list(motif_df, extrainfo = TRUE, force = FALSE)
requires_update(motifs, extrainfo = TRUE)
```

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#### **Arguments**

motifs List of motifs.

extrainfo Use the extrainfo slot in the tidy data.frame. The column names will be

taken from the character vectors themselves, and unnamed elements will be assigned a unique name. To add elements to the slot, simply create new columns in the data.frame. Note that these will be coerced into characters. If extrainfo is not set to TRUE in to\_df(), then the contents of the slot will not be transferred to the data.frame. If extrainfo is not set to TRUE in update\_motifs() or

to\_list(), then the extra columns will be discarded.

motif\_df Motif data.frame generated by to\_df().

force Whether to coerce non-character data types into characters for inclusion in extrainfo.

If force is FALSE (the default), columns which are not of type "character", "numeric", or "integer" (for example, list columns, or logical values), will not be added to the motif extrainfo slot, but will be passed onto the returned universalmotif\_df unchanged. Setting force = TRUE coerces these values

into a character, adding them to the extrainfo slot, and updating the universalmotif\_df

columns to reflect this coercion. In other words, forcing inclusion of these data

is destructive and will change the column values. Use with caution.

#### **Details**

To turn off the informative messages/warnings when printing the object to the console, set options(universalmotif\_df.wa

#### Value

```
For to_df(): a data.frame with the exposed slots as columns.
```

For update\_motifs(): the updated data.frame.

For requires\_update(): TRUE if the motifs are out of date, FALSE if otherwise. Note that this function uses identical() to check for this, which can be quite slow for large datasets. It is usually just as fast to simply run update\_motifs() in such cases.

For to\_list(): a list of motifs.

## Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

```
## Not run:
library(universalmotif)
library(dplyr)

m <- c(create_motif(name = "motif A"), create_motif(name = "motif B"))

# Change the names of the motifs using the tidy way:
m <- m %>%
    to_df() %>%
    mutate(name = paste0(name, "-2")) %>%
```

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```
to_list()

# Add your own metadata to be stored in the extrainfo slot:
m_df <- to_df(m)
m_df$MyMetadata <- c("Info_1", "Info_2")
m <- to_list(m_df, extrainfo = TRUE)

## End(Not run)</pre>
```

trim\_motifs

Trim motifs.

## **Description**

Remove edges of motifs with low information content. Currently does not trim multifreq representations.

# Usage

```
trim_motifs(motifs, min.ic = 0.25, trim.from = c("both", "left", "right"))
```

# Arguments

motifs See convert\_motifs() for acceptable formats.

min.ic numeric(1) Minimum allowed information content. See convert\_type() for

a discussion on information content.

trim.from character(1) Control the direction of trimming.

#### Value

Motifs See convert\_motifs() for available output formats.

### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## See Also

```
create_motif(), convert_type()
```

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universalmotif-class universalmotif: Motif class.

### **Description**

Container for motif objects. See create\_motif() for creating motifs as well as a more detailed description of the slots. For a brief description of available methods, see examples.

# Usage

```
## S4 method for signature 'universalmotif'
x[i]
## S4 replacement method for signature 'universalmotif'
x[i] \leftarrow value
## S4 method for signature 'universalmotif'
initialize(.Object, name, altname, family, organism,
  motif, alphabet = "DNA", type, icscore, nsites, pseudocount = 1, bkg,
  bkgsites, consensus, strand = "+-", pval, qval, eval, multifreq, extrainfo,
  gapinfo)
## S4 method for signature 'universalmotif'
show(object)
## S4 method for signature 'universalmotif'
as.data.frame(x)
## S4 method for signature 'universalmotif'
subset(x, select)
## S4 method for signature 'universalmotif'
normalize(object)
## S4 method for signature 'universalmotif'
rowMeans(x)
## S4 method for signature 'universalmotif'
colMeans(x)
## S4 method for signature 'universalmotif'
colSums(x)
## S4 method for signature 'universalmotif'
rowSums(x)
## S4 method for signature 'universalmotif'
```

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```
nrow(x)
## S4 method for signature 'universalmotif'
ncol(x)
## S4 method for signature 'universalmotif'
colnames(x)
## S4 method for signature 'universalmotif'
rownames(x)
## S4 method for signature 'universalmotif'
cbind(..., deparse.level = 0)
```

# **Arguments**

x universalmotif Motif.

i character Slot.

value Object to replace slot with.

.Object universalmotif Final motif.

name character(1) Motif name.

altname character(1) Alternate motif name.

family character(1) Transcription factor family.

organism character(1) Species of origin.

motif matrix Each column represents a position in the motif.

alphabet character(1) One of c('DNA', 'RNA', 'AA'), or a combined string represent-

ing the letters.

type character(1) One of c('PCM', 'PPM', 'PWM', 'ICM').

icscore numeric(1) Total information content. Automatically generated. nsites numeric(1) Number of sites the motif was constructed from.

pseudocount numeric(1) Correction to be applied to prevent -Inf from appearing in PWM

matrices.

bkg numeric A vector of probabilities, each between 0 and 1. If higher order back-

grounds are provided, then the elements of the vector must be named.

bkgsites numeric(1) Total number of sites used to find the motif.

consensus character(1) Consensus string. Automatically generated for 'DNA', 'RNA',

and 'AA' alphabets.

strand character(1) Whether the motif is specific to a certain strand.

pval numeric(1) P-value associated with motif.

qval numeric(1) Adjusted P-value associated with motif.

eval numeric(1) E-value associated with motif.

multifreq list See add\_multifreq().

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```
extrainfo character Any other extra information, represented as a named character vector.

gapinfo universalmotif_gapped(1) Gapped motif information.

object universalmotif Motif.

select numeric Columns to keep.

... universalmotif Motifs.

deparse.level Unused.
```

#### Value

A motif object of class universalmotif.

## **Slots**

```
name character(1)
altname character(1)
family character(1)
organism character(1)
motif matrix
alphabet character(1)
type character(1)
icscore numeric(1) Generated automatically.
nsites numeric(1)
pseudocount numeric(1)
bkg numeric 0-order probabilities must be provided for all letters.
bkgsites numeric(1)
consensus character Generated automatically.
strand character(1)
pval numeric(1)
qval numeric(1)
eval numeric(1)
multifreq list
extrainfo character
gapinfo universalmotif_gapped(1)
```

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

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```
## [
## Access the slots.
motif <- create_motif()</pre>
motif["motif"]
# you can also access multiple slots at once, released as a list
motif[c("motif", "name")]
## 「<-
## Replace the slots.
motif["name"] <- "new name"</pre>
# some slots are protected
# motif["consensus"] <- "AAAA" # not allowed</pre>
## Assemble a list of motifs.
c(motif, motif)
## as.data.frame
## Represent a motif as a data.frame. The actual motif matrix is lost.
## Necessary for `summarise_motifs`.
as.data.frame(motif)
## subset
## Subset a motif matrix by column.
subset(motif, 3:7) # extract motif core
## normalize
## Apply the pseudocount slot (or `1`, if the slot is set to zero) to the
## motif matrix.
motif2 <- create_motif("AAAAA", nsites = 100, pseudocount = 1)</pre>
normalize(motif2)
## rowMeans
## Calculate motif rowMeans.
rowMeans(motif)
## colMeans
## Calculate motif colMeans.
colMeans(motif)
## colSums
## Calculate motif colSums
colSums(motif)
## rowSums
## Calculate motif rowSums.
rowSums(motif)
## nrow
## Count motif rows.
nrow(motif)
```

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```
## ncol
## Count motif columns.
ncol(motif)

## colnames
## Get motif colnames.
colnames(motif)

## rownames
## Get motif rownames.
rownames(motif)

## cbind
## Bind motifs together to create a new motif.
cbind(motif, motif2)
```

universalmotif-pkg

universalmotif: Import, Modify and Export Motifs with R

# **Description**

A collection of utility functions for working with motifs.

utilities

Utility functions.

# Description

Utility functions have been split into two categories: those related to motifs ?'utils-motif', and those related to sequences ?'utils-sequence'.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

# See Also

utils-motif, utils-sequence

utils-motif

*Motif-related utility functions.* 

## Description

Motif-related utility functions.

## Usage

```
add_gap(motif, gaploc = ncol(motif)%/%2, mingap = 1, maxgap = 5)
average_ic(motifs, average = c("a.mean", "g.mean", "median", "fzt"))
compare_columns(x, y, method, bkg1 = rep(1/length(x), length(x)),
  bkg2 = rep(1/length(y), length(y)), nsites1 = 100, nsites2 = 100)
consensus_to_ppm(letter)
consensus_to_ppmAA(letter)
get_consensus(position, alphabet = "DNA", type = "PPM", pseudocount = 1)
get_consensusAA(position, type = "PPM", pseudocount = 0)
get_matches(motif, score, allow.nonfinite = FALSE)
get_scores(motif, allow.nonfinite = FALSE)
icm_to_ppm(position)
motif_range(motif, use.freq = 1, allow.nonfinite = FALSE)
motif\_score(motif, threshold = c(0, 1), use.freq = 1,
  allow.nonfinite = FALSE, threshold.type = c("total", "fromzero"))
log_string_pval(pval)
pcm_to_ppm(position, pseudocount = 0)
position_icscore(position, bkg = numeric(), type = "PPM",
  pseudocount = 1, nsites = 100, relative_entropy = FALSE,
  schneider_correction = FALSE)
ppm_to_icm(position, bkg = numeric(), schneider_correction = FALSE,
  nsites = 100, relative_entropy = FALSE)
ppm_to_pcm(position, nsites = 100)
```

```
ppm_to_pwm(position, bkg = numeric(), pseudocount = 1, nsites = 100,
    smooth = TRUE)

prob_match(motif, match, allow.zero = TRUE)

prob_match_bkg(bkg, match)

pwm_to_ppm(position, bkg = numeric())

round_motif(motif, pct.tolerance = 0.05)

score_match(motif, match, allow.nonfinite = FALSE)

summarise_motifs(motifs, na.rm = TRUE)

ungap(motif, delete = FALSE)
```

# Arguments

motif	Motif object to calculate scores from, or add/remove gap, or round.
gaploc	numeric Motif gap locations. The gap occurs immediately after every position value. If missing, uses round(ncol(motif) / 2).
mingap	numeric Minimum gap size. Must have one value for every location. If missing, set to 1.
maxgap	numeric Maximum gap size. Must have one value for every location. If missing, set to 5.
motifs	list A list of universalmotif motifs.
average	character(1) One of $c("a.mean", "g.mean", "median", "fzt")$ . How to calculate the average motif information content.
X	numeric First column for comparison.
У	numeric Second column for comparison.
method	character(1) Column comparison metric. See compare_motifs() for details.
bkg1	numeric Vector of background probabilities for the first column. Only relevant if $method = "ALLR"$ .
bkg2	numeric Vector of background probabilities for the second column. Only relevant if method = "ALLR".
nsites1	<pre>numeric(1) Number of sites for the first column. Only relevant if method = "ALLR".</pre>
nsites2	<pre>numeric(1) Number of sites for the second column. Only relevant if method = "ALLR".</pre>
letter	character(1) Any DNA, RNA, or AA IUPAC letter. Ambiguity letters are accepted.
position	numeric A numeric vector representing the frequency or probability for each alphabet letter at a specific position.

alphabet character(1) One of c('DNA', 'RNA').

type character(1) One of c('PCM', 'PPM', 'PWM' 'ICM').

pseudocount numeric(1) Used to prevent zeroes in motif matrix.

score numeric(1) Logodds motif score.

allow.nonfinite

logical(1) If FALSE, then apply a pseudocount if non-finite values are found in the PWM. Note that if the motif has a pseudocount greater than zero and the motif is not currently of type PWM, then this parameter has no effect as the pseudocount will be applied automatically when the motif is converted to a PWM internally. This value is set to FALSE by default in order to stay consistent with pre-version 1.8.0 behaviour. A message will be printed if a pseudocount is applied. To disable this, set options (pseudocount.warning=FALSE).

use.freq numeric(1) Use regular motif or the respective multifreq representation.

threshold numeric(1) Any number of numeric values between 0 and 1 representing score

percentage.

threshold.type character For "total", a threshold of zero represents the minimum possible

score. This means the range of scores that can be extracted is from the minimum to the maximum possible scores. For "fromzero", a threshold of zero is a score of zero. This means the range of scores is from zero to the maximum. The "total" threshold type can only be used if no non-finite values are present in

the PWM.

pval character(1) String-formatted p-value.

bkg numeric Should be the same length as the alphabet length.

nsites numeric(1) Number of sites motif originated from.

relative\_entropy

logical(1) Calculate information content as relative entropy or Kullback-Leibler

divergence.

schneider\_correction

logical(1) Apply sample size correction.

smooth logical(1) Apply pseudocount correction.

match character Sequence string to calculate score from.

allow.zero logical(1) If FALSE, apply a pseudocount if zero values are found in the back-

ground frequencies.

pct.tolerance numeric(1) or character(1) The minimum tolerated proportion each letter

must represent per position in order not to be rounded off, either as a numeric value from 0 to 1 or a percentage written as a string from "0%" to "100%".

na.rm logical Remove columns where all values are NA.

delete logical(1) Clear gap information from motif. If FALSE, then it can be reacti-

vated simply with add\_gap(motif).

## Value

```
For consensus_to_ppm() and consensus_to_ppmAA(): a numeric vector of length 4 and 20, respectively.

For get_consensus() and get_consensusAA(): a character vector of length 1.

For get_matches(): a character vector of motif matches.

For motif_range(): a named numeric vector of motif scores.

For motif_score(): a named numeric vector of length 1.

For log_string_pval(): a numeric vector of length 1.

For position_icscore(): a numeric vector of length 1.

For ppm_to_icm(), icm_to_ppm(), pcm_to_ppm(), ppm_to_pcm(), ppm_to_pwm(), and pwm_to_ppm(): a numeric vector with length equal to input numeric vector.

For prob_match(): a numeric vector of probabilities.

For round_motif(): the input motif, rounded.

For score_match(): a numeric vector with the match motif score.

For summarise_motifs(): a data.frame with columns representing the universalmotif slots.
```

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## See Also

```
create_motif()
```

```
data(examplemotif)
examplemotif0 <- examplemotif
examplemotif0["pseudocount"] <- 0
## add_gap
## Add gap information to a motif.
m <- create_motif()</pre>
# Add a gap size 5-8 between positions 4 and 5:
m <- add_gap(m, gaploc = 4, mingap = 5, maxgap = 8)
## average_ic
## Calculate the average information content for a list of motifs.
m <- create_motif()</pre>
average_ic(m, "fzt")
## compare_columns
## Compare two numeric vectors using the metrics from compare_motifs()
compare_columns(c(0.5, 0.1, 0.1, 0.2), c(0.7, 0.1, 0.1, 0.1), "PCC")
```

```
## consensus_to_ppm
## Do the opposite of get_consensus. Note that loss of information is
## inevitable. Generates a sequence matrix.
sapply(c("A", "G", "T", "B"), consensus_to_ppm)
## consensus_to_ppmAA
## Do the opposite of get_consensusAA and generate a motif matrix.
sapply(c("V", "A", "L"), consensus_to_ppmAA)
## get_consensus
## Get a consensus string from a DNA/RNA motif.
m <- create_motif()["motif"]</pre>
apply(m, 2, get_consensus)
## get consensusAA
## Get a consensus string from an amino acid motif. Unless each position
## is clearly dominated by a single amino acid, the resulting string will
## likely be useless.
m <- create_motif(alphabet = "AA")["motif"]</pre>
apply(m, 2, get_consensusAA, type = "PPM")
## get_match
## Get all possible motif matches above input score
get_matches(examplemotif, 0)
get_matches(examplemotif0, 0, allow.nonfinite = TRUE)
## get_scores
## Get all possible scores for a motif
length(get_scores(examplemotif))
get_scores(examplemotif)
get_scores(examplemotif0, allow.nonfinite = TRUE)
## icm_to_ppm
## Do the opposite of ppm_to_icm.
m <- create_motif(type = "ICM")["motif"]</pre>
apply(m, 2, icm_to_ppm)
## motif_range
## Calculate the range of possible logodds scores for a motif
motif_range(examplemotif)
motif_range(examplemotif, allow.nonfinite = TRUE)
## motif_score
```

```
## Calculate motif score from different thresholds
m <- normalize(examplemotif)</pre>
motif\_score(m, c(0, 0.8, 1))
motif_score(examplemotif0, c(0, 0.8, 1), allow.nonfinite = TRUE,
  threshold.type = "fromzero")
## log_string_pval
## Get the log of a string-formatted p-value
log_string_pval("1e-200")
## pcm_to_ppm
## Go from a count type motif to a probability type motif.
m <- create_motif(type = "PCM", nsites = 50)["motif"]</pre>
apply(m, 2, pcm_to_ppm, pseudocount = 1)
## position_icscore
## Similar to ppm_to_icm, except this calculates the position sum.
m <- create_motif()["motif"]</pre>
apply(m, 2, position_icscore, type = "PPM", bkg = rep(0.25, 4))
## ppm_to_icm
## Convert one column from a probability type motif to an information
## content type motif.
m <- create_motif(nsites = 100, pseudocount = 0.8)["motif"]</pre>
apply(m, 2, ppm_to_icm, nsites = 100, bkg = rep(0.25, 4))
## ppm_to_pcm
## Do the opposite of pcm_to_ppm.
m <- create_motif()["motif"]</pre>
apply(m, 2, ppm_to_pcm, nsites = 50)
## ppm_to_pwm
## Go from a probability type motif to a weight type motif.
m <- create_motif()["motif"]</pre>
apply(m, 2, ppm_to_pwm, nsites = 100, bkg = rep(0.25, 4))
## prob_match, prob_match_bkg
## Calculate probability of a particular match based on background
## frequencies
prob_match(examplemotif, "TATATAT")
## Since this motif has a uniform background, the probability of
## finding any motif hit within the sequence is equal
prob_match(examplemotif, "TATATAG")
m <- examplemotif
m["bkg"] \leftarrow c(0.3, 0.2, 0.2, 0.3)
prob_match(m, "TATATAT")
```

```
## The prob_match_bkg alternative allows you to simply pass along the
## background frequencies
prob_match_bkg(c(A=0.3, C=0.2, G=0.2, T=0.3), c("TATATAT", "TATATAG"))
## pwm_to_ppm
## Do the opposite of ppm_to_pwm.
m <- create_motif(type = "PWM")["motif"]</pre>
apply(m, 2, pwm_to_ppm, bkg = rep(0.25, 4))
## Note that not all type conversions can be done directly; for those
## type conversions which are unavailable, universalmotif just chains
## together others (i.e. from PCM -> ICM => pcm_to_ppm -> ppm_to_icm)
## round_motif
## Round down letter scores to 0 \,
m <- create_motif()</pre>
## Remove letters from positions which are less than 5% of the total
## position:
round_motif(m, pct.tolerance = 0.05)
## score_match
## Calculate score of a particular match
score_match(examplemotif, "TATATAT")
score_match(examplemotif, "TATATAG")
score_match(examplemotif0, "TATATAT", allow.nonfinite = TRUE)
score_match(examplemotif0, "TATATAG", allow.nonfinite = TRUE)
## summarise_motifs
## Create a data.frame of information based on a list of motifs.
m1 <- create_motif()</pre>
m2 <- create_motif()</pre>
m3 <- create_motif()</pre>
summarise_motifs(list(m1, m2, m3))
## Unset motif's gap status. Does not delete actual gap data unless
## delete = TRUE.
m <- create_motif()</pre>
m < - add_gap(m, 3, 2, 4)
m <- ungap(m)</pre>
# Restore gap data:
m <- add_gap(m)</pre>
```

## **Description**

Sequence-related utility functions.

#### Usage

```
calc_complexity(string, complexity.method = c("WoottonFederhen",
  "WoottonFederhenFast", "Trifonov", "TrifonovFast", "DUST"), alph = NULL,
  trifonov.max.word.size = 7)
calc_windows(n, window = 1, overlap = 0, return.incomp = TRUE)
count_klets(string, k = 1, alph)
get_klets(lets, k = 1)
mask_ranges(seqs, ranges, letter = "-")
mask_seqs(seqs, pattern, RC = FALSE, letter = "-")
meme_alph(core, file = stdout(), complements = NULL, ambiguity = NULL,
  like = NULL, alph.name = NULL, letter.names = NULL, colours = NULL)
shuffle_string(string, k = 1, method = c("euler", "linear", "markov"),
  rng.seed = sample.int(10000, 1))
slide_fun(string, FUN, FUN.VALUE, window = 1, overlap = 0,
  return.incomp = TRUE)
window_string(string, window = 1, overlap = 0, return.incomp = TRUE,
  nthreads = 1)
```

## **Arguments**

character (1) A character vector containing a single string, with the exception string of calc\_complexity() where string can be a length greater than one. complexity.method character(1) Complexity algorithm. See sequence\_complexity(). alph character (1) A single character string with the desired sequence alphabet. If missing, finds the unique letters within each string. trifonov.max.word.size integer(1) Maximum word size for use in the Trifonov complexity methods. See sequence\_complexity(). integer(1) Total size from which to calculate sliding windows. n window integer(1) Window size to slide along. overlap integer(1) Overlap size between windows.

return.incomp logical(1) Whether to return the last window if it is smaller then the requested window size.

k integer(1) K-let size.

lets character A character vector where each element will be considered a single

unit.

seqs XStringSet Sequences to mask. Cannot be BStringSet.

ranges GRanges The ranges to mask. Must be a GRanges object from the GenomicRanges

package.

letter character (1) Character to use for masking.

pattern character(1) Pattern to mask.

RC logical(1) Whether to mask the reverse complement of the pattern.

core character(1) Core alphabet symbols. If complements are also provided, then

only half of the letters should be provided to this argument.

file Output file.

complements character(1), NULL Complementary letters to the core symbols.

ambiguity character(1), NULL A named vector providing ambiguity codes for the custom

alphabet.

like character(1), NULL How to classify the custom alphabet. If not NULL, then one

of c("DNA", "RNA", "PROTEIN").

alph.name character(1), NULL Custom alphabet name.

letter.names character, NULL Named vector of core symbol names.

colours character, NULL Named vector of core symbol colours. MEME requires hex

colours.

method character(1) Shuffling method. One of c("euler", "linear", "markov").

See shuffle\_sequences().

rng.seed numeric(1) Set random number generator seed. Since shuffling in shuffle\_sequences()

can occur simultaneously in multiple threads using C++, it cannot communicate with the regular R random number generator state and thus requires an independent seed. Since shuffle\_string() uses the same underlying code as shuffle\_sequences(), it also requires a separate seed even if it is run in serial.

FUN closure The function to apply per window. (See ?vapply.)

FUN. VALUE The expected return type for FUN. (See ?vapply.)

nthreads integer(1) Number of threads to use. Zero uses all available threads.

#### Value

For calc\_complexity(): A vector of numeric values.

For calc\_windows(): A data.frame with columns start and stop.

For count\_klets(): A data.frame with columns lets and counts.

For get\_klets(): A character vector of k-lets.

For mask\_ranges(): The masked XStringSet object.

For mask\_seqs(): The masked XStringSet object.

For meme\_alph(): NULL, invisibly.

```
For shuffle_string(): A single character string.
For slide_fun(): A vector with type FUN. VALUE.
For window_string(): A character vector.
```

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
create_sequences(), get_bkg(), sequence_complexity(), shuffle_sequences()
```

```
## calc complexity
## Calculate complexity for abitrary strings
calc_complexity("GTGCCCCGCGGGAACCCCGC", c = "WoottonFederhen")
calc_complexity("GTGCCCCGCGGGAACCCCGC", c = "WoottonFederhenFast")
calc_complexity("GTGCCCCGCGGGAACCCCGC", c = "Trifonov")
calc_complexity("GTGCCCCGCGGGAACCCCGC", c = "TrifonovFast")
calc_complexity("GTGCCCCGCGGGAACCCCGC", c = "DUST")
## calc_windows
## Calculate window coordinates for any value 'n'.
calc_windows(100, 10, 5)
## count_klets
## Count k-lets for any string of characters
count_klets("GCAAATGTACGCAGGGCCGA", k = 2)
## The default 'k' value (1) counts individual letters
count_klets("GCAAATGTACGCAGGGCCGA")
## get_klets
## Generate all possible k-lets for a set of characters
get_klets(c("A", "C", "G", "T"), 3)
## Note that each element in 'lets' is considered a single unit;
get_klets(c("AA", "B"), k = 2)
## mask_ranges
## Mask arbitrary ranges
if (requireNamespace("GenomicRanges", quiet = TRUE)) {
ranges <- GenomicRanges::GRanges("A", IRanges::IRanges(1, 5))</pre>
seq <- Biostrings::DNAStringSet(c(A = "ATGACTGATTACTTATA"))</pre>
mask_ranges(seq, ranges, "-")
}
```

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```
## mask_seqs
## Mask repetitive sequences
data(ArabidopsisPromoters)
mask_seqs(ArabidopsisPromoters, "AAAAAA")
## Create MEME custom alphabet definition files
meme_alph("ACm", complements = "TGM", alph.name = "MethDNA",
 letter.names = c(A = "Adenine", C = "Cytosine", G = "Guanine",
  T = "Thymine", m = "Methylcytosine", M = "mC:Guanine"),
 like = "DNA", ambiguity = c(N = "ACGTmM"))
## shuffle_string
## Shuffle any string of characters
shuffle\_string("ASDADASDASDASD", k = 1)
## slide_fun
## Apply a function to a character vector along sliding windows
FUN <- function(x) grepl("[GC]", x)</pre>
data.frame(
 Window = window_string("ATGCATCTATGCA", 2, 1),
 HasGC = slide_fun("ATGCATCTATGCA", FUN, logical(1), 2, 1)
## window_string
## Get sliding windows for a string of characters
window_string("ABCDEFGHIJ", 2, 1)
```

view\_logo

Plot logos from numeric matrices.

#### **Description**

This function provides the plotting capabilities of view\_motifs() without requiring universalmotifclass objects. Instead, it takes a numeric matrix with row names as input. Additionally, columns can be of any height and letters can be a mix of different character lengths.

## Usage

```
view_logo(x, fontDF = NULL, fill = "black", colour.scheme = NULL,
min.height = 0.01, x.spacer = 0.04, y.spacer = 0.01,
sort.positions = FALSE, sort.positions.decreasing = TRUE,
fit.to.height = NULL)
```

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# Arguments

X	A numeric matrix with row names. The row names can be a mix of different character lengths.
fontDF	data.frame or DataFrame Polygon data for letters used for plotting, as generated by the createPolygons() function from the gglogo package. See the fontDFroboto data object (which is used by default when fontDF = NULL). See Examples for how to generate your own font set. Expected columns: x, y, order, group; additional columns will be ignored.
fill	character $\boldsymbol{A}$ single colour to fill all letters with. Ignored if colour.scheme is provided.
colour.scheme	character A named character vector of colour names. Provide colours for individual letters, even if the row names are made up of multiple characters.
min.height	numeric(1) Minimum height for a letter to be plotted. The number is taken as the fraction of the total height of the plot. The default value is to not show letters which take up 1% or less of the vertical space. For smaller figures it is recommended to increase this value, and vice versa for larger figures.
x.spacer	numeric(1) Add horizontal spacing between letters. The number is taken as the fraction of the width of an individual position. Increasing this value is recommended for letters made up of multiple characters.
y.spacer	numeric(1) Add vertical spacing between letters. The number is taken as the fraction nof the total height of the plot.
sort.positions	logical(1) Sort letters vertically per position by height.
sort.positions	
	logical(1) Sort in decreasing or increasing order based on letter height.
fit.to.height	numeric(1) Normalize the per position height to this value. If NULL, no normalization is applied. Note that this parameter is ignored if use.type = $c("PWM", "ICM")$ .

## Value

A ggplot object. If you wish to plot the data yourself from polygon paths, access them using \$data on the output object. The theme theme\_void() is applied to the object; apply your own theme or adjust specific plot parameters with theme() to change this.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

# See Also

view\_motifs()

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# **Examples**

```
## Feel free to mix and match row name character lengths and column sums.
data(examplemotif)
toplot <- examplemotif["motif"]
toplot[4] <- 2
toplot[20] <- -0.5
rownames(toplot)[1] <- "AA"
view_logo(toplot)</pre>
```

view\_motifs

Plot motif logos.

# Description

Show sequence logo. If given a list of more than one motif, then the motifs are aligned with the first in the list.

## Usage

```
view_motifs(motifs, use.type = "ICM", method = "ALLR", tryRC = TRUE,
min.overlap = 6, min.mean.ic = 0.25, relative_entropy = FALSE,
normalise.scores = FALSE, min.position.ic = 0, score.strat = "sum",
return.raw = FALSE, dedup.names = TRUE, show.positions = TRUE,
show.positions.once = TRUE, show.names = TRUE, names.pos = c("top",
"right"), use.freq = 1, colour.scheme = NULL, fontDF = NULL,
min.height = 0.01, x.spacer = if (use.freq == 1) 0.04 else 0.1,
y.spacer = 0.01, sort.positions = !use.type %in% c("PCM", "PPM"),
sort.positions.decreasing = TRUE, text.size = 16, fit.to.height = if
(use.type == "PPM") 1 else NULL, RC.text = " [RC]", ...)
```

# **Arguments**

motifs	See convert_motifs() for acceptable motif formats.
use.type	character(1) One of c('PCM', 'PPM', 'PWM', 'ICM').
method	character(1) One of PCC, EUCL, SW, KL, ALLR, BHAT, HELL, SEUCL, MAN, ALLR_LL, WEUCL, WPCC. See details.
tryRC	logical(1) Try the reverse complement of the motifs as well, report the best score.
min.overlap	numeric(1) Minimum overlap required when aligning the motifs. Setting this to a number higher then the width of the motifs will not allow any overhangs. Can also be a number between 0 and 1, representing the minimum fraction that the motifs must overlap.

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min.mean.ic

numeric(1) Minimum mean information content between the two motifs for an alignment to be scored. This helps prevent scoring alignments between low information content regions of two motifs. Note that this can result in some comparisons failing if no alignment passes the mean IC threshold. Use <a href="https://www.average\_ic">average\_ic()</a>) to filter out low IC motifs to get around this if you want to avoid getting NAs in your output.

relative\_entropy

logical(1) Change the ICM calculation affecting min.position.ic and min.mean.ic. See convert\_type().

normalise.scores

logical(1) Favour alignments which leave fewer unaligned positions, as well as alignments between motifs of similar length. Similarity scores are multiplied by the ratio of aligned positions to the total number of positions in the larger motif, and the inverse for distance scores.

min.position.ic

numeric(1) Minimum information content required between individual alignment positions for it to be counted in the final alignment score. It is recommended to use this together with normalise.scores = TRUE, as this will help punish scores resulting from only a fraction of an alignment.

score.strat

character(1) How to handle column scores calculated from motif alignments. "sum": add up all scores. "a.mean": take the arithmetic mean. "g.mean": take the geometric mean. "median": take the median. "wa.mean", "wg.mean": weighted arithmetic/geometric mean. "fzt": Fisher Z-transform. Weights are the total information content shared between aligned columns.

return.raw

logical(1) Instead of returning a plot, return the aligned named matrices used to generate the plot. This can be useful if you wish to use view\_motifs() alignment capabilities for custom plotting uses. Alignment is performed by adding empty columns to the left or right of motifs to generate matrices of equal length.

dedup.names

logical(1) Plotting motifs with duplicated names is not allowed. Setting this to TRUE allows the names to be modified for plotting.

show.positions logical(1) Show x-axis position tick labels.

show.positions.once

logical(1) When plotting multiple motifs, show x-axis position tick labels only once. If FALSE, then x-axis tick labels are specific to each motif.

show.names

logical(1) Add motif names when plotting multiple motifs.

names.pos

character(1) Motif name locations. Either above (top) or to the right (right) of the logos.

use.freq

numeric(1) Plot higher order motifs from the multifreq slot.

colour.scheme

character A named character vector of colour names. Default colours are provided for DNA, RNA, and AA motifs if left NULL.

fontDF

data.frame or DataFrame Polygon data for letters used for plotting, as generated by the createPolygons() function from the gglogo package. See the fontDFroboto data object (which is used by default when fontDF = NULL). See Examples for how to generate your own font set. Expected columns: x, y, order, group; additional columns will be ignored.

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min.height	numeric(1) Minimum height for a letter to be plotted. The number is taken as the fraction of the total height of the plot. The default value is to not show letters which take up 1% or less of the vertical space. For smaller figures it is recommended to increase this value, and vice versa for larger figures.
x.spacer	numeric(1) Add horizontal spacing between letters. The number is taken as the fraction of the width of an individual position. Increasing this value is recommended for plotting multifreq motifs.
y.spacer	numeric(1) Add vertical spacing between letters. The number is taken as the fraction nof the total height of the plot.
sort.positions	logical(1) Sort letters vertically per position by height.
sort.positions.	
	logical(1) Sort in decreasing or increasing order based on letter height.
text.size	numeric(1) Text size for labels.
fit.to.height	numeric(1) Normalize the per position height to this value. If NULL, no normalization is applied. Note that this parameter is ignored if use.type = c("PWM", "ICM").
RC.text	character(1) The text to display alongside the name of motifs shown as their reverse complement.
	Unused. Was previously in place to allow extra args to be given to ggseqlogo: :ggseqlogo, however universalmotif now implements its own motif plotting code directly with ggplot2.

# **Details**

See compare\_motifs() for more info on comparison parameters.

See view\_logo() to plot from a numeric matrix with arbitrary values instead of a motif object.

Note: score.strat = "a.mean" is NOT recommended, as view\_motifs() will not discriminate between two alignments with equal mean scores, even if one alignment is longer than the other.

Note: if you want to plot the motifs yourself, you can set return.raw=TRUE to get the numeric motif matrices and calculate the polygon paths on your own or access the polygon path data directly from the final ggplot object using \$data.

# Value

A ggplot object. If return.raw = TRUE, a list of matrices.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
compare_motifs(), add_multifreq(), view_logo()
```

write\_homer 91

## **Examples**

```
## Plotting multifreq motifs:
data(examplemotif2)
view_motifs(examplemotif2, use.freq = 2)
## Generate your own letter set:
## Not run:
library(gglogo) # install from CRAN first if needed
fontDFtimes <- createPolygons(LETTERS, "Times", 800, scale = TRUE)</pre>
view_motifs(examplemotif2, fontDF = fontDFtimes)
## Note: setting `scale = TRUE` is necessary to properly align letters
## vertically, but this has the effect of horizontally stretching out
## letters which shouldn't be stretched (such as "I"). If you need to plot
## letters which have been badly horizontally scaled, you can fix them
## manually as demonstrated here:
# Retrieve the x-coordinates for the desired letter:
tofix <- fontDFtimes$x[fontDFtimes$group == "I"]</pre>
# Scale the letter x-coordinates:
tofix <- tofix * 0.35
# Remember to center the letter around 0.5 again:
tofix <- tofix + (1 - max(tofix)) / 2
# Apply the fix:
fontDFtimes$x[fontDFtimes$group == "I"] <- tofix</pre>
view_motifs(create_motif("AIG", alphabet = "AA"), fontDF = fontDFtimes)
## End(Not run)
```

write\_homer

Export motifs in HOMER format.

## Description

Convert DNA motifs to HOMER format and write to file. See <a href="http://homer.ucsd.edu/homer/motif/">http://homer.ucsd.edu/homer/motif/</a>.

# Usage

```
write_homer(motifs, file, logodds_threshold = NULL, overwrite = FALSE,
append = FALSE, threshold = 0.8, threshold.type = c("logodds",
   "logodds.abs", "pvalue"))
```

92 write\_homer

## **Arguments**

motifs See convert\_motifs() for acceptable formats.

file character(1) File name.

logodds\_threshold

Deprecated. If set, read\_homer() will behave like pre-version 1.12.0 of the universalmotif package for backwards compatibility (though a warning will

be printed).

overwrite logical(1) Overwrite existing file.

append logical(1) Add to an existing file.

threshold numeric(1) Stringency required for HOMER to match a motif. See scan\_sequences()

for how to use this argument. Can be a single value to be recycled for all motifs,

or a vector of equal length to the number of motifs.

threshold.type character(1) How the threshold value should be used to obtain the final

threshold value in the written motif. See scan\_sequences() for how to use

this.

#### Value

NULL, invisibly.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## References

Heinz S, Benner C, Spann N, Bertolino E, Lin YC, Laslo P, Cheng JX, Murre C, Singh H, Glass CK (2010). "Simple combinations of lineage-determining transcription factors prime cis-regulatory elements required for macrophage and B cell identities." *Molecular Cell*, **38**, 576-589.

## See Also

```
read_homer()
```

Other write\_motifs: write\_jaspar(), write\_matrix(), write\_meme(), write\_motifs(), write\_transfac()

```
motif <- create_motif()
write_homer(motif, tempfile())</pre>
```

write\_jaspar 93

|--|

## **Description**

Convert motifs to JASPAR format and write to file. See <a href="http://jaspar.genereg.net/">http://jaspar.genereg.net/</a>.

# Usage

```
write_jaspar(motifs, file, overwrite = FALSE, append = FALSE)
```

## **Arguments**

```
motifs See convert_motifs() for acceptable formats.
```

file character(1) File name.

overwrite logical(1) Overwrite existing file.
append logical(1) Add to an existing file.

#### Value

NULL, invisibly.

# Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## References

Khan A, Fornes O, Stigliani A, Gheorghe M, Castro-Mondragon JA, van der Lee R, Bessy A, Cheneby J, Kulkarni SR, Tan G, Baranasic D, Arenillas DJ, Sandelin A, Vandepoele K, Lenhard B, Ballester B, Wasserman WW, Parcy F, Mathelier A (2018). "JASPAR 2018: update of the open-access database of transcription factor binding profiles and its web framework." *Nucleic Acids Research*, **46**, D260-D266.

#### See Also

```
read_jaspar()
```

```
Other write_motifs: write_homer(), write_matrix(), write_meme(), write_motifs(), write_transfac()
```

94 write\_matrix

# **Description**

Write motifs as simple matrices with optional headers to file.

# Usage

```
write_matrix(motifs, file, positions = "columns", rownames = FALSE, type,
  sep = "", headers = TRUE, overwrite = FALSE, append = FALSE,
  digits = 6)
```

# Arguments

motifs	See convert_motifs() for acceptable formats.
file	character(1) File name.
positions	character(1) One of c('columns', 'rows'). Partial matching allowed.
rownames	logical(1) Include alphabet letters as rownames.
type	character(1) One of c('PCM', 'PPM', 'PWM', 'ICM'). If missing will use whatever type the motif is currently stored as.
sep	character(1) Indicates how to separate individual motifs. Set as NULL to have no seperating lines between motifs (the default is to use a blank line).
headers	logical(1), character(1) Indicating if and how to write names.
overwrite	logical(1) Overwrite existing file.
append	logical(1) Add to an existing file.
digits	numeric(1) Number of digits to use for motif positions.

## Value

NULL, invisibly.

## Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### See Also

```
read_matrix()
Other write_motifs: write_homer(), write_jaspar(), write_meme(), write_motifs(), write_transfac()
```

```
motif <- create_motif()
write_matrix(motif, tempfile(), headers = ">")
```

write\_meme 95

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Export motifs in MEME format.

## **Description**

Convert motifs to minimal MEME format and write to file. See <a href="http://meme-suite.org/doc/meme-format.html">http://meme-suite.org/doc/meme-format.html</a>.

#### **Usage**

```
write_meme(motifs, file, version = 5, bkg, strand, overwrite = FALSE,
   append = FALSE)
```

## **Arguments**

motifs See convert\_motifs() for acceptable formats.

file character(1) File name.
version numeric(1) MEME version.

bkg numeric Background letter frequencies. If missing, will use background fre-

quencies from motif objects (if they are identical); else background frequencies

will be set to freq = 1/length(alphabet)

strand character If missing, will use strand from motif objects (if identical); other-

wise will default to "+ -"

overwrite logical(1) Overwrite existing file.

append logical(1) Add to an existing file. Motifs will be written in minimal format,

so it is recommended to only use this if the existing file is also a minimal MEME

format file.

#### Value

NULL, invisibly.

## Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

#### References

Bailey TL, Boden M, Buske FA, Frith M, Grant CE, Clementi L, Ren J, Li WW, Noble WS (2009). "MEME SUITE: tools for motif discovery and searching." *Nucleic Acids Research*, **37**, W202-W208.

#### See Also

```
read_meme()
```

Other write\_motifs: write\_homer(), write\_jaspar(), write\_matrix(), write\_motifs(), write\_transfac()

96 write\_motifs

## **Examples**

write\_motifs

Export motifs in universalmotif format.

# Description

Write motifs as universalmotif objects to file. For optimal storage of universalmotif class motifs, consider using saveRDS() and readRDS(). Currently the universalmotif format is YAML-based, but this is subject to change.

# Usage

```
write_motifs(motifs, file, minimal = FALSE, multifreq = TRUE,
    progress = FALSE, overwrite = FALSE, append = FALSE, BP = FALSE)
```

## **Arguments**

motifs	See convert_motifs() for acceptable formats.
file	character(1) File name.
minimal	logical(1) Only write essential motif information.
multifreq	logical(1) Write multifreq slot, if present.
progress	logical(1) Show progress.
overwrite	logical(1) Overwrite existing file.
append	logical(1) Add to an existing motif file. Package version in existing motif file must be greater than 1.2.0.
BP	logical(1) Allows for the use of <b>BiocParallel</b> within write_motifs(). See

BiocParallel::register() to change the default backend.

#### Value

NULL, invisibly.

#### Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## See Also

```
Other write_motifs: write_homer(), write_jaspar(), write_matrix(), write_meme(), write_transfac()
```

write\_transfac 97

write_transfac	Export motifs in TRANSFAC format.	

## **Description**

Convert motifs to TRANSFAC format and write to file.

# Usage

```
write_transfac(motifs, file, overwrite = FALSE, append = FALSE,
  name.tag = "ID", altname.tag = "NA")
```

## **Arguments**

motifs See convert\_motifs() for acceptable formats.

file character(1) File name.

overwrite logical(1) Overwrite existing file.
append logical(1) Add to an existing file.

name.tag character(1) The tag to use when writing the motifs name slot.

altname.tag character(1) The tag to use when writing the motifs altname slot. Note that

no tag will be written if the slot is empty.

#### **Details**

If the family slot of a motif is not empty, then its contents will included using the HC tag. Similarly for the organism slot using the tag OS. The default name and alternate name tags are ID and NA, respectively, though these can be set manually.

## Value

NULL, invisibly.

## Author(s)

Benjamin Jean-Marie Tremblay, <benjamin.tremblay@uwaterloo.ca>

## References

Wingender E, Dietze P, Karas H, Knuppel R (1996). "TRANSFAC: A Database on Transcription Factors and Their DNA Binding Sites." *Nucleic Acids Research*, **24**, 238-241.

#### See Also

```
read_transfac()
```

```
Other write_motifs: write_homer(), write_jaspar(), write_matrix(), write_meme(), write_motifs()
```

98 write\_transfac

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