

Package ‘scanMiR’

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Type Package

Title scanMiR

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Description A set of tools for working with miRNA affinity models (KdModels), efficiently scanning for miRNA binding sites, and predicting target repression. It supports scanning using miRNA seeds, full miRNA sequences (enabling 3' alignment) and KdModels, and includes the prediction of slicing and TDMD sites. Finally, it includes utility and plotting functions (e.g. for the visual representation of miRNA-target alignment).

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aggregateMatches	<i>aggregateMatches</i>
------------------	-------------------------

Description

Aggregates miRNA binding sites with log_kd values to predict transcript repression. See the vignette for more detail.

Usage

```
aggregateMatches(
  m,
  a = 0.007726,
  b = 0.5735,
  c = 0.181,
  p3 = 0.051,
  coef_utr = 0,
  coef_orf = 0,
  p3.range = c(3L, 8L),
  keepSiteInfo = TRUE,
  toInt = FALSE,
  BP = NULL
)
```

Arguments

<code>m</code>	A GRanges or data.frame of matches as returned by 'findSeedMatches'.
<code>a</code>	The relative concentration of unbound AGO-miRNA complexes.
<code>b</code>	Factor specifying the additional repression by a single bound AGO.
<code>c</code>	Penalty for sites that are found within the ORF region.
<code>p3</code>	Factor specifying additional repression due to 3p alignment.
<code>coef_utr</code>	Factor specifying additional repression due to UTR length.
<code>coef_orf</code>	Factor specifying additional repression due to ORF length.
<code>p3.range</code>	Range used for 3p alignment.
<code>keepSiteInfo</code>	Logical; whether to return information about site types (default = TRUE). Ignored if 'm' does not contain 'log_kd' values
<code>toInt</code>	Logical; whether to convert repression scores to integers (default = FALSE).
<code>BP</code>	Pass 'BiocParallel::MulticoreParam(ncores, progressbar=TRUE)' to enable multithreading. Note that in addition, 'aggregateMatches' uses the data.table package, which is often set to use multi-threading by default (which would be multiplied by threads determined by 'BP'). See setDTthreads for more information.

Value

a data.frame containing aggregated repression values and/or information about the numbers and types of matches

Examples

```
# we create mock RNA sequences and seeds:
seqs <- getRandomSeq(n=10)

# load sample KdModel
data(SampleKdModel)

# find matches
matches <- findSeedMatches(seqs, SampleKdModel)

# aggregate matches
aggregateMatches(matches)
```

assignKdType

assignKdType

Description

Assigns a log_kd and match type to a set of matched sequences.

Usage

```
assignKdType(x, mod, mer8 = NULL)
```

Arguments

x	A vector of matched sequences, each of 12 nucleotides
mod	An object of class 'KdModel'
mer8	The optional set of 8mers included in the model (for internal use; can be reconstructed from the model).

Value

A data.frame with one row for each element of 'x', and the columns 'type' and 'log_kd'. To save space, the reported log_kd is multiplied by 1000, rounded and saved as an integer.

Examples

```
data(SampleKdModel)
assignKdType(c("CTAGCATTAAAGT", "ACGTACGTACGT"), SampleKdModel)
```

conservation

conservation

Description

conservation

Usage

```
conservation(x)
```

Arguments

x	A KdModelList, or a KdModel
---	-----------------------------

Value

A vector of the conservation status for each miRNA

Examples

```
data(SampleKdModel)
conservation(SampleKdModel)
```

dummyKdData	<i>Create dummy log_kd per 12-mer data</i>
-------------	--

Description

Create dummy log_kd per 12-mer data

Usage

```
dummyKdData(mod = NULL)
```

Arguments

mod Optional model from which to create the dummy data

Value

A data.frame with 12-mers and log_kds

Examples

```
kd <- dummyKdData()
```

findSeedMatches	<i>Predicting and characterizing miRNA binding sites</i>
-----------------	--

Description

‘findSeedMatches’ takes a set of sequences and a set of miRNAs (given either as target seeds, mature miRNA sequences, or a [KdModelList](#)).

Usage

```
findSeedMatches(  
  seqs,  
  seeds,  
  shadow = 0L,  
  onlyCanonical = FALSE,  
  maxLogKd = c(-1, -1.5),  
  keepMatchSeq = FALSE,  
  minDist = 7L,  
  p3.extra = FALSE,  
  p3.params = list(maxMirLoop = 7L, maxTargetLoop = 9L, maxLoopDiff = 4L, mismatch =  
    TRUE, GUwob = TRUE),  
  agg.params = .defaultAggParams(),  
  ret = c("GRanges", "data.frame", "aggregated"),  
  BP = NULL,  
  verbose = NULL,  
  n_seeds = NULL,  
  useTmpFiles = FALSE,  
  keepTmpFiles = FALSE  
)
```

Arguments

seqs	A character vector or 'DNAStrngSet' of DNA sequences in which to look.
seeds	A character vector of 7-nt seeds to look for. If RNA, will be reversed and complemented before matching. If DNA, they are assumed to be the target sequence to look for. Alternatively, a list of objects of class 'KdModel' or an object of class 'KdModelList' can be given.
shadow	Integer giving the shadow, i.e. the number of nucleotides hidden at the beginning of the sequence (default 0).
onlyCanonical	Logical; whether to restrict the search only to canonical binding sites.
maxLogKd	Maximum log_kd value to keep. This has a major impact on the number of sites returned, and hence on the memory requirements. Set to Inf to disable (not recommended when running large scans!).
keepMatchSeq	Logical; whether to keep the sequence (including flanking dinucleotides) for each seed match (default FALSE).
minDist	Integer specifying the minimum distance between matches of the same miRNA (default 7). Closer matches will be reduced to the highest-affinity. To disable the removal of overlapping features, use 'minDist=-Inf'.
p3.extra	Logical; whether to keep extra information about 3' alignment. Disable (default) this when running large scans, otherwise you might hit your system's memory limits.
p3.params	Named list of parameters for 3' alignment with slots 'maxMirLoop' (integer, default = 7), 'maxTargetLoop' (integer, default = 9), 'maxLoopDiff' (integer, default = 4), 'mismatch' (logical, default = TRUE) and 'GUwob' (logical, default = TRUE).
agg.params	A named list with slots 'a', 'b', 'c', 'p3', 'coef_utr', 'coef_orf' and 'keepSite-Info' indicating the parameters for the aggregation. Ignored if 'ret!="aggregated"'. For further details see documentation of 'aggregateMatches'.
ret	The type of data to return, either "GRanges" (default), "data.frame", or "aggregated" (aggregates affinities/sites for each seed-transcript pair).
BP	Pass 'BiocParallel::MulticoreParam(ncores, progressbar=TRUE)' to enable multithreading.
verbose	Logical; whether to print additional progress messages (default on if not multithreading)
n_seeds	Integer; the number of seeds that are processed in parallel to avoid memory issues.
useTmpFiles	Logical; whether to write results for single miRNAs in temporary files (ignored when scanning for a single seed). Alternatively, 'useTmpFiles' can be a character vector of length 1 indicating the path to the directory in which to write temporary files.
keepTmpFiles	Logical; whether to keep the temporary files at the end of the process; ignored if 'useTmpFiles=FALSE'. Temporary files are removed only upon successful completion of the function, meaning that they will not be deleted in case of errors.

Value

A GRanges of all matches. If 'seeds' is a 'KdModel' or 'KdModelList', the 'log_kd' column will report the ln(Kd) multiplied by 1000, rounded and saved as an integer. If 'ret!="GRanges', returns a data.frame.

Examples

```
# we create mock RNA sequences and seeds:
seqs <- getRandomSeq(n=10)
seeds <- c("AAACCAC", "AAACCUU")
findSeedMatches(seqs, seeds)
```

get3pAlignment	<i>Finds 3' complementary binding of a miRNA</i>
----------------	--

Description

Performs a local alignment of the miRNA 3' sequence (determined by 'mir3p.start') on given the given sequences.

Usage

```
get3pAlignment(
  seqs,
  mirseq,
  mir3p.start = 9L,
  allow.mismatch = TRUE,
  maxMirLoop = 7L,
  maxTargetLoop = 9L,
  maxLoopDiff = 4L,
  TGsub = TRUE,
  siteType = NULL
)
```

Arguments

seqs	A set of sequences in which to look for 3' matches (i.e. upstream of the seed match)
mirseq	The sequence of the mature miRNA
mir3p.start	The position in 'mirseq' in which to start looking
allow.mismatch	Logical; whether to allow mismatches
maxMirLoop	Maximum miRNA loop size
maxTargetLoop	Maximum target loop size
maxLoopDiff	Maximum size difference between miRNA and target loops
TGsub	Logical; whether to allow T/G substitutions.
siteType	The optional type of seed-complementarity, as returned by getMatchTypes . This is needed to identify slicing/TDMD sites. If given, should be a vector of the same length as 'seqs'.

Value

A data.frame with one row for each element of 'seqs', indicating the size of the miRNA bulge, the size of the target mRNA bulge, the number of mismatches at the 3' end, and the partial 3' alignment score (i.e. roughly the number of consecutive matching nucleotides)

Examples

```
get3pAlignment(seqs="NNAGTGTGCCATNN", mirseq="TGGAGTGTGACAATGGTGTGG")
```

```
get8merRange          get8merRange
```

Description

Returns the minimum and maximum 8-mer log-kd values

Usage

```
get8merRange(mod)
```

Arguments

mod A 'KdModel'

Value

A numeric vector of length two

Examples

```
data("SampleKdModel")
get8merRange(SampleKdModel)
```

```
getKdModel            getKdModel
```

Description

getKdModel

Usage

```
getKdModel(kd, mirseq = NULL, name = NULL, conservation = NA_integer_, ...)
```

Arguments

kd	A data.frame containing the log_kd per 12-mer sequence, or the path to a text/csv file containing such a table. Should contain the columns 'log_kd', '12mer' (or 'X12mer'), and eventually 'mirseq' (if the 'mirseq' argument is NULL) and 'mir' (if the 'name' argument is NULL).
mirseq	The miRNA (cDNA) sequence.
name	The name of the miRNA.
conservation	The conservation level of the miRNA. See 'scanMiR:::conservation_levels()' for possible values.
...	Any additional information to be saved with the model.

Value

An object of class 'KdModel'.

Examples

```
kd <- dummyKdData()
mod <- getKdModel(kd=kd, mirseq="TTAATGCTAATCGTGATAGGGTT", name="my-miRNA")
```

getKmers

getKmers

Description

Returns all combinations of 'n' elements of 'from'

Usage

```
getKmers(n = 4, from = c("A", "C", "G", "T"))
```

Arguments

n	Number of elements
from	Letters sampled

Value

A character vector

Examples

```
getKmers(3)
```

getMatchTypes

getMatchTypes

Description

Given a seed and a set of sequences matching it, returns the type of match.

Usage

```
getMatchTypes(x, seed, checkWobble = TRUE)
```

Arguments

x	A character vector of short sequences.
seed	A 7 or 8 nucleotides string indicating the seed (5' to 3' sequence of the target RNA). If of length 7, an "A" will be appended.
checkWobble	Whether to flag wobbled sites

Value

A factor of match types.

Examples

```
x <- c("AACACTCCAG", "GAACTCCGC", "GTACTCCAT", "ACGTACGTAC")
getMatchTypes(x, seed="AACTCCA")
```

getRandomSeq	<i>getRandomSeq</i>
--------------	---------------------

Description

Produces a random sequence of the given letters

Usage

```
getRandomSeq(length = 3000, alphabet = c("A", "C", "G", "T"), n = 1)
```

Arguments

length	Length of the sequence
alphabet	Letters from which to sample
n	The number of sequences to generate

Value

A character vector of length 1

Examples

```
getRandomSeq(100)
```

getSeed8mers	<i>getSeed8mers</i>
--------------	---------------------

Description

Generates all possible 8mers with 4 consecutive and positioned matches to a given seed.

Usage

```
getSeed8mers(seed, addNs = FALSE)
```

Arguments

seed	The miRNA seed (target DNA sequence), a character vector of length 8 (if of length 7, a "A" will be added on the right)
addNs	Logical; whether to include 8mers with one flanking N

Value

A vector of 1024 8mers.

Examples

```
head(getSeed8mers("ACACTCCA"))
```

KdModel	<i>miRNA affinity models</i>
---------	------------------------------

Description

Methods for the [KdModel](#) class

Usage

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

```
## S4 method for signature 'KdModel'  
summary(object)
```

```
## S4 method for signature 'KdModel'  
c(x, ...)
```

Arguments

object, x, ... An object of class [KdModel](#)

Value

Depends on the method.

See Also

[KdModel](#), [KdModelList](#)

Examples

```
data(SampleKdModel)  
SampleKdModel  
summary(SampleKdModel)
```

KdModelList-class *KdModelList*

Description

KdModelList

Usage

```
KdModelList(..., description = NULL, makeUnique = FALSE)
```

Arguments

... Any number of [KdModel](#) objects or lists thereof.
description A description for the collection.
makeUnique Logical; whether to rename models if names are duplicated.

Value

A KdModelList

Examples

```
data(SampleKdModel)
mods <- KdModelList(SampleKdModel, SampleKdModel, makeUnique = TRUE)
mods
```

KdModelList-methods *Methods for the [KdModelList](#) classes*

Description

Methods for the [KdModelList](#) classes

Usage

```
## S4 method for signature 'KdModelList'
summary(object)

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

Arguments

object, x An object of class [KdModelList](#)
i the index of item(s) to select
j, drop, ... ignored

Value

Depends on the method.

See Also

[KdModel](#), [KdModelList](#)

Examples

```
# create a KdModelList :
data(SampleKdModel)
kml <- KdModelList( SampleKdModel, SampleKdModel, makeUnique=TRUE )
summary(kml)
kml[1] # returns a KdModelList
kml[[2]] # returns a KdModel
conservation(kml)
```

plotKdModel

plotKdModel

Description

Plots the summary of an affinity model.

Usage

```
plotKdModel(mod, what = c("both", "seeds", "logo"), n = 10)
```

Arguments

mod	A ‘KdModel’
what	Either ‘seeds’, ‘logo’, or ‘both’ (default).
n	The number of top 7-mers to plot (when ‘what=’seeds’)

Details

‘what=’seeds‘ plots the $-\log(K_d)$ values of the top ‘n’ 7-mers (including both canonical and non-canonical sites), with or without the final "A" vis-a-vis the first miRNA nucleotide. ‘what=’logo‘ plots a ‘seqLogo’ (requires the [seqLogo]<https://bioconductor.org/packages/release/bioc/html/seqLogo.html> package) showing the nucleotide-wise information content and preferences for all 12-mers (centered around the seed, oriented in the direction of the target mRNA). ‘what="both"‘ plots both. Note that if the package ‘ggseqlogo’ is installed, this will be used instead to plot the logo, resulting in more detailed plot annotation.

Value

If ‘what="logo"‘, returns nothing and plots a position weight matrix. Otherwise returns a ggplot.

Examples

```
data(SampleKdModel)
plotKdModel(SampleKdModel, what="seeds")
```

```
removeOverlappingRanges
      removeOverlappingRanges
```

Description

Removes elements from a GRanges that overlap (or are within a given distance of) other elements higher up in the list (i.e. assumes that the ranges are sorted in order of priority). The function handles overlaps between more than two ranges by successively removing those that overlap higher-priority ones.

Usage

```
removeOverlappingRanges(
  x,
  minDist = 7L,
  retIndices = FALSE,
  ignore.strand = FALSE
)
```

Arguments

<code>x</code>	A GRanges, sorted by (decreasing) importance.
<code>minDist</code>	Minimum distance between ranges.
<code>retIndices</code>	Logical; whether to return the indices of entries to remove, rather than the filtered GRanges.
<code>ignore.strand</code>	Logical. Whether the strand of the input ranges should be ignored or not.

Value

A filtered GRanges, or an integer vector of indices to be removed if 'retIndices==TRUE'.

Examples

```
library(GenomicRanges)
gr <- GRanges(seqnames=rep("A",4), IRanges(start=c(10,25,45,35), width=6))
removeOverlappingRanges(gr, minDist=7)
```

SampleKdModel	<i>Example KdModel (hsa-miR-155-5p)</i>
---------------	---

Description

'KdModel' for hsa-miR-155-5p, based on Kd predictions from the CNN of [McGeary, Lin et al. (2019)](<https://dx.doi.org/10.1126/science.aav1741>).

Value

a 'KdModel' object

Examples

```
data(SampleKdModel)
SampleKdModel
```

SampleTranscript	<i>Example transcript sequence</i>
------------------	------------------------------------

Description

An artificial transcript sequence used for examples.

Value

a named character vector of length 1.

viewTargetAlignment	<i>viewTargetAlignment</i>
---------------------	----------------------------

Description

viewTargetAlignment

Usage

```
viewTargetAlignment(
  m,
  miRNA,
  seqs = NULL,
  flagBulgeMatches = FALSE,
  p3.params = list(),
  min3pMatch = 3L,
  hideSingletons = FALSE,
  UGsub = TRUE,
  ...,
  outputType = c("print", "data.frame", "plot", "ggplot")
)
```

Arguments

m	A GRanges of length 1 giving the information for a given match, as produced by findSeedMatches .
miRNA	A miRNA sequence, or a KdModel object of the miRNA corresponding to the match in 'm'; alternatively, a KdModelList including the model.
seqs	The sequences corresponding to the seqnames of 'm'. Not needed if 'm' contains the target sequences.
flagBulgeMatches	Logical; whether to flag matches inside the bulge (default FALSE)
p3.params	See findSeedMatches .

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