

Package ‘EpiTxDb’

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Type Package

Title Storing and accessing epitranscriptomic information using the AnnotationDbi interface

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Description EpiTxDb facilitates the storage of epitranscriptomic information. More specifically, it can keep track of modification identity, position, the enzyme for introducing it on the RNA, a specifier which determines the position on the RNA to be modified and the literature references each modification is associated with.

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Imports methods, utils, httr, xml2, curl, rex, GenomicFeatures, txdbmaker, GenomicRanges, GenomeInfoDb, BiocGenerics, BiocFileCache, S4Vectors, IRanges, RSQLite, DBI, Biostrings, tRNAdbImport

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Collate 'AllGenerics.R' 'EpiTxDb-SELECT-helpers.R' 'EpiTxDb-schema.R' 'EpiTxDb.R' 'EpiTxDb-class.R' 'makeEpiTxDb.R' 'makeEpiTxDbFromGRanges.R' 'shiftGenomicToTranscript.R' 'makeEpiTxDbFromRMBase.R' 'makeEpiTxDbFromtRNAdb.R' 'modifications.R' 'modificationsBy.R' 'ranges-helpers.R' 'select-methods.R'

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EpiTxDb-package	<i>EpiTxDb: Storing and accessing epitranscriptomic information using the AnnotationDbi interface</i>
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Description

EpiTxDb facilitates the storage of epitranscriptomic information. More specifically, it can keep track of modification identity, position, the enzyme for introducing it on the RNA, a specifier which determines the position on the RNA to be modified and the literature references each modification is associated with.

Author(s)

Maintainer: Felix G.M. Ernst <felix.gm.ernst@outlook.com> (ORCID)

See Also

Useful links:

- <https://github.com/FelixErnst/EpiTxDb>
- Report bugs at <https://github.com/FelixErnst/EpiTxDb/issues>

EpiTxDb-class

EpiTxDb objects

Description

The EpiTxDb class is a [AnnotationDb](#) type container for storing Epitranscriptomic information.

The information are typically stored on a per transcript and not as genomic coordinates, but the EpiTxDb class is agnostic to this. In case of genomic coordinates transcriptsBy will return modifications per chromosome.

Usage

```
## S4 method for signature 'EpiTxDb'  
organism(object)
```

```
## S4 method for signature 'EpiTxDb'  
seqinfo(x)
```

```
## S4 method for signature 'EpiTxDb'  
seqlevels(x)
```

```
## S4 method for signature 'EpiTxDb'  
as.list(x)
```

Arguments

x, object a EpiTxDb object

Value

For

- organism() and seqlevels() a character vector
- seqinfo() a [Seqinfo](#) object
- as.list() a list

See Also

- [makeEpiTxDbFromGRanges](#) for creating a EpiTxDb object from a [GRanges](#) object and it's metadata columns
- [makeEpiTxDbFromRMBase](#) for creating a EpiTxDb object from RMBase online resources
- [makeEpiTxDbFromtRNadb](#) for creating a EpiTxDb object from tRNadb online resources
- [makeEpiTxDb](#) for creating a EpiTxDb object from `data.frames`
- [modifications](#), [modificationsBy](#) for getting epitranscriptomic modification locations
- [select](#) for using the default interface of [AnnotationDb](#) objects.
- [shiftGenomicToTranscript](#) and [shiftTranscriptToGenomic](#) for transferring genomic to transcript coordinates and back again.

Examples

```
etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNadb.sqlite",
                        package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb

# general methods
seqinfo(etdb) #
seqlevels(etdb) # easy access to all transcript names
```

EpiTxDb-data

EpiTxDb internal data

Description

EpiTxDb internal data

Usage

```
data(rmbase_data)
```

Format

`data.frame`

EpiTxDb-package#'	EpiTxDb - <i>Storing and accessing epitranscriptomic information using the AnnotationDbi interface</i>
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Description

title

Author(s)

Felix G M Ernst [aut]

References

Jia-Jia Xuan, Wen-Ju Sun, Ke-Ren Zhou, Shun Liu, Peng-Hui Lin, Ling-Ling Zheng, Liang-Hu Qu, Jian-Hua Yang (2017): "RMBase v2.0: Deciphering the Map of RNA Modifications from Epitranscriptome Sequencing Data." *Nucleic Acids Research*, Volume 46, Issue D1, 4 January 2018, Pages D327–D334. doi: 10.1093/nar/gkx934

Jühling, Frank; Mörl, Mario; Hartmann, Roland K.; Sprinzl, Mathias; Stadler, Peter F.; Pütz, Joern (2009): "TRNAdb 2009: Compilation of tRNA Sequences and tRNA Genes." *Nucleic Acids Research* 37 (suppl_1): D159–D162. doi: 10.1093/nar/gkn772

Sprinzl, Mathias; Vassilenko, Konstantin S. (2005): "Compilation of tRNA Sequences and Sequences of tRNA Genes." *Nucleic Acids Research* 33 (suppl_1): D139–D140. doi: 10.1093/nar/gki012

makeEpiTxDb	<i>Creating a EpiTxDb from user supplied annotations as data.frames</i>
-------------	---

Description

makeEpiTxDb is a low-level constructor for creating a [EpiTxDb](#) object from user supplied annotations.

This functions typically will not be used by regular users.

Usage

```
makeEpiTxDb(
  modifications,
  reactions = NULL,
  specifiers = NULL,
  references = NULL,
  metadata = NULL,
  reassign.ids = FALSE
)
```

Arguments

- modifications** A data.frame containing the following columns:
- **mod_id**: a unique integer value per modification.
 - **mod_type**: the modification type as a character or factor value. Must be a value from `shortName(ModRNAString())`.
 - **mod_name**: a character or factor name for the specific modification
 - **mod_start**: the start position for the modification as integer value. Usually `mod_start = mod_end`
 - **mod_end**: the end position for the modification as integer value. Usually `mod_start = mod_end`
 - **mod_strand**: the strand information for the modification as a character or factor.
 - **sn_id**: a integer value per unique sequence
 - **sn_name**: a character or factor as sequence name, e.g a chromosome or a transcript identifier like `chr1`.
- The first six are mandatory, whereas one of the last two has to be set. `sn_id` will be generated from `sn_name`, if `sn_id` is not set.
- reactions** An optional data.frame containing the following columns:
- **mod_id**: a integer value per modification and the link to the modification data.frame.
 - **rx_genename**: a character or factor referencing a genename for the enzyme incorporating the modification.
 - **rx_rank**: a integer for sorting enzyme reactions, if multiple enzymes are involved in the modification's incorporation/maintenance.
 - **rx_ensembl**: a character or factor with an ensembl identifier for the genename of the enzyme.
 - **rx_ensembltrans**: a character or factor with an ensembl identifier for the transcript being translated into the enzyme.
 - **rx_entrezid**: a character or factor with an entrezid for the genename of the enzyme.
- (default: `reactions = NULL`)
- specifiers** An optional data.frame containing the following columns:
- **mod_id**: a integer value per modification and the link to the modification data.frame.
 - **spec_type**: a character or factor referencing a type of specifier, e.g. `snoRNA`. Not checked for validity.
 - **spec_genename**: a character or factor referencing a genename for the specifier directing an enzyme to the specific location for the modification to be incorporated.
 - **spec_ensembl**: a character or factor with an ensembl identifier for the genename of the specifier.
 - **spec_ensembltrans**: a character or factor with an ensembl identifier for the transcript being translated into the specifier.

	• <code>spec_entrezid</code>: a character or factor with an entrezid for the gene-name of the specifier. (default: <code>specifiers = NULL</code>)
<code>references</code>	An optional <code>data.frame</code> containing the following columns: • <code>mod_id</code>: a integer value per modification and the link to the modification <code>data.frame</code>. • <code>ref_type</code>: a character or factor with a reference type, e.g. PMID. Is not checked for validity. • <code>ref</code>: a character or factor with a reference value, e.g. a specific pubmed id or an journal article. Is not checked for validity. (default: <code>references = NULL</code>)
<code>metadata</code>	An optional <code>data.frame</code> containing the following columns: • <code>name</code>: a character value used as name • <code>value</code>: a character value This dataframe will be returned by <code>metadata()</code> (default: <code>metadata = NULL</code>)
<code>reassign.ids</code>	TRUE or FALSE Controls how internal <code>mod_ids</code> should be assigned. If <code>reassign.ids</code> is FALSE (the default) and if the ids are supplied, then they are used as the internal ids, otherwise the internal ids are assigned in a way that is compatible with the order defined by ordering the modifications first by chromosome, then by strand, then by start, and finally by end.

Value

a `EpiTxDb` object.

See Also

- [makeEpiTxDbFromGRanges](#) for creating a `EpiTxDb` object from a `GRanges` object and it's metadata columns
- [makeEpiTxDbFromRMBase](#) for creating a `EpiTxDb` object from RMBase online resources
- [makeEpiTxDbFromtRNadb](#) for creating a `EpiTxDb` object from tRNadb online resources
- [shortName](#) and [ModRNAString](#) for information on `ModRNAString` objects.

Examples

```
mod <- data.frame("mod_id" = 1L,
                  "mod_type" = "m1A",
                  "mod_name" = "m1A_1",
                  "mod_start" = 1L,
                  "mod_end" = 1L,
                  "mod_strand" = "+",
                  "sn_id" = 1L,
                  "sn_name" = "test")
rx <- data.frame(mod_id = 1L,
                 rx_genename = "test",
                 rx_rank = 1L,
```

```

      rx_ensembl = "test",
      rx_ensembltrans = "test",
      rx_entrezid = "test")
spec <- data.frame(mod_id = 1L,
                  spec_type = "test",
                  spec_genename = "test",
                  spec_ensembl = "test",
                  spec_ensembltrans = "test",
                  spec_entrezid = "test")
ref <- data.frame(mod_id = 1L,
                  ref_type = "test",
                  ref = "test")
etdb <- makeEpiTxDb(mod,rx,spec,ref)

```

makeEpiTxDbFromGRanges

Create a EpiTxDb object from a GRanges object

Description

makeEpiTxDbFromGRanges extracts informations from a [GRanges](#) object. The following metadata columns can be used:

- mod_id, mod_type, mod_name and tx_ensembl. The first three are mandatory, whereas tx_ensembl is optional.
- rx_genename, rx_rank, rx_ensembl, rx_ensembltrans and rx_entrezid
- spec_type, spec_genename, spec_ensembl, spec_ensembltrans and spec_entrezid
- ref_type and ref

... and passed on the [makeEpiTxDb](#).

Usage

```
makeEpiTxDbFromGRanges(gr, metadata = NULL, reassign.ids = FALSE)
```

Arguments

gr	A GRanges object, which contains at least the mandatory columns.
metadata	A 2-column data.frame containing meta information to be included in the EpiTxDb object. This data.frame is just passed to makeEpiTxDb . See makeEpiTxDb for more information about the format of metadata. (default: metadata = NULL)
reassign.ids	= FALSE

Value

a EpiTxDb object.

Examples

```
library(GenomicRanges)
gr <- GRanges(seqnames = "test",
              ranges = IRanges::IRanges(1,1),
              strand = "+",
              DataFrame(mod_id = 1L,
                       mod_type = "Am",
                       mod_name = "Am_1"))
etdb <- makeEpiTxDbFromGRanges(gr)
```

makeEpiTxDbFromRMBase *Create a EpiTxDb object from RMBase v2.0 online resources*

Description

makeEpiTxDbFromRMBase will make use of the RMBase v2.0 online resources.

Usage

EPITXDB_RMBASE_URL

downloadRMBaseFiles(organism, genome, modtype)

```
makeEpiTxDbFromRMBase(
  organism,
  genome,
  modtype,
  tx = NULL,
  sequences = NULL,
  metadata = NULL,
  reassign.ids = FALSE,
  verbose = FALSE
)
```

getRMBaseDataAsGRanges(files, verbose = FALSE)

```
makeEpiTxDbFromRMBaseFiles(
  files,
  tx = NULL,
  sequences = NULL,
  metadata = NULL,
  reassign.ids = FALSE,
  verbose = FALSE
)
```

listAvailableOrganismsFromRMBase()

```
listAvailableGenomesFromRMBase(organism)
```

```
listAvailableModFromRMBase(organism, genome)
```

Arguments

organism	A character value, which must match an organism descriptor on the RMBase download website.
genome	A character value, which must match a genome descriptor on the RMBase download website.
modtype	A character value, which must match one or more modification descriptors on the RMBase download website.
tx	A GRangesList object which will be used to shift the genomic coordinates to transcript coordinates. This is optional, but highly recommended. (default: tx = NULL).
sequences	A named DNAStringSet or RNAStringSet , which will be used to check whether the defined modifications are compatible with the original base. This uses removeIncompatibleModifications function from the Modstrings package.
metadata, reassign.ids	See makeEpiTxDb
verbose	TRUE or FALSE: Should verbose message be printed?
files	From organism, genome and modtype the available files will be downloaded using the BiocFileCache interface and passed on to makeEpiTxDbFromRMBaseFiles . However, individual files can be provided as well.

Format

An object of class character of length 1.

Value

a EpiTxDb object.

`makeEpiTxDbFromtRNAdb` *Create a EpiTxDb object from tRNAdb resources*

Description

`makeEpiTxDbFromtRNAdb` will make use of the tRNAdb online resources and extract the modification information from the RNA database.

If a named [DNAStringSet](#) is provided as sequences, the result from the tRNAdb will be matched against the sequences. Valid matches will be used as transcript identifiers and returned after a check of modification compatibility with the provided sequence. By this process multiple copies of transcripts can be associated with a single modification.

`makeEpiTxDbFromtRNAdb` uses the functions provided by the [tRNAdbImport](#) package. `import.tRNAdb` will be used with `database = "RNA"` and the three different values for origin.

Usage

```
gettRNAdbDataAsGRanges(  
  organism,  
  sequences = NULL,  
  dbURL = tRNAdbImport::TRNA_DB_URL  
)  
  
makeEpiTxDbFromtRNAdb(  
  organism,  
  sequences = NULL,  
  metadata = NULL,  
  dbURL = tRNAdbImport::TRNA_DB_URL  
)  
  
listAvailableOrganismsFromtRNAdb()
```

Arguments

organism	A character value for an organism available on the tRNAdb website.
sequences	A named DNASTringSet or RNASTringSet, which will be used to associate a tRNAdb result with a specific transcript.
dbURL	The URL to the tRNA db website.
metadata	See makeEpiTxDb

Value

a EpiTxDb object.

References

Juehling F, Moerl M, Hartmann RK, Sprinzl M, Stadler PF, Puetz J. 2009. "tRNAdb 2009: compilation of tRNA sequences and tRNA genes." Nucleic Acids Research, Volume 37 (suppl_1): D159–162. doi:10.1093/nar/gkn772.

Examples

```
## Not run:  
# getting just the annotation data  
etdb <- makeEpiTxDbFromtRNAdb("Saccharomyces cerevisiae")  
  
# For associating the result with transcripts, provide and additional  
# named DNASTringSet object. Matching will be done against each sequence  
# allowing 5 mismatches and indels. The final result will be checked for  
# validity regarding the identity of the modifications  
etdb <- makeEpiTxDbFromtRNAdb("Saccharomyces cerevisiae",  
                             some_transcript_sequences)  
  
## End(Not run)
```

modifications

*Getting modification data from a EpiTxDb-object***Description**

modifications and modificationsBy are functions to extract modification annotation from a [EpiTxDb](#) object.

modifiedSeqsByTranscript returns a [ModRNAStringSet](#) from a EpiTxDb object and compatible RNAStringSet object. This used the [combineIntoModstrings\(\)](#) function from the Modstrings package.

Usage

```
modifications(
  x,
  columns = c("mod_id", "mod_type", "mod_name"),
  filter = NULL,
  use.names = FALSE,
  ...
)

modificationsBy(
  x,
  by = c("seqnames", "mod_type", "reaction", "specifier", "specifier_type"),
  ...
)

modifiedSeqsByTranscript(x, sequences, ...)

## S4 method for signature 'EpiTxDb'
modifications(
  x,
  columns = c("mod_id", "mod_type", "mod_name"),
  filter = NULL,
  use.names = FALSE
)

## S4 method for signature 'EpiTxDb'
modificationsBy(
  x,
  by = c("seqnames", "modtype", "reaction", "specifier", "specifiertype")
)

## S4 method for signature 'EpiTxDb,DNAStringSet'
modifiedSeqsByTranscript(x, sequences)
```

Arguments

x	a EpiTxDb
columns	Columns to include in the result. If the vector is named, those names are used for the corresponding column in the element metadata of the returned object. (default: columns = c("mod_id", "mod_type", "mod_name"))
filter	Either NULL or a named list of vectors to be used to restrict the output. Valid names for this list are: "mod_id", "mod_type", "mod_name", "sn_id", "sn_name", "rx_genename", "rx_ensembl", "rx_ensembltrans", "rx_entrezid", "spec_genename", "spec_type", "spec_ensembl", "spec_ensembltrans", "spec_entrezid", "ref_type" and "ref". (default: filter = NULL)
use.names	TRUE or FALSE. If TRUE, the modification names are set as the names of the returned object. (default: use.names = FALSE)
...	Not used.
by	By which information type should the result be split into? A character value from one of the following values: • seqnames • mod_type • reaction • specifier • specifier_type
sequences	A RNAStringSet, which can be used as input for combineIntoModstrings() . See ?combineIntoModstrings for additional details.

Value

a [GRanges](#) object for modifications and a [GRangesList](#) for modificationsBy.

Examples

```
etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNAdb.sqlite",
                        package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb
```

positionSequence	<i>Generate integer sequences from position information of Ranges</i>
------------------	---

Description

positionSequence generates sequences of integer values along the range information of x. This can be used for navigating specific positions on a range information.

Usage

```

positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'Ranges'
positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'RangesList'
positionSequence(x, order = FALSE, decreasing = FALSE)

## S4 method for signature 'Ranges'
as.integer(x)

```

Arguments

x	a Ranges object, like a GRanges or IRanges , or a RangesList object, like a GRangesList or IRangesList
order	TRUE or FALSE: Should the position be ordered? (default: order = FALSE)
decreasing	TRUE or FALSE: If order = TRUE Should the position be ordered in a decreasing order? (default: order = FALSE)

Value

a integer vector if x is a [GRanges](#) object and a IntegerList if x is a [GRangesList](#)

Examples

```

library(GenomicRanges)
# Returns an integer vector
gr <- GRanges("chr1:1-5:+")
positionSequence(gr)
gr2 <- GRanges("chr1:1-5:-")
positionSequence(gr)
# returns an IntegerList
grl <- GRangesList("1" = gr, "2" = gr, "3" = gr2) # must be named
positionSequence(grl)

```

rescale

Rescaling Ranges object

Description

rescale() rescales IRanges, GRanges, IRangesList and GRangesList by using minima and maxima derived from to and from.

Usage

```
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'IRanges'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'IRangesList'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'GRanges'
rescale(x, to = 1L, from = 1L)

## S4 method for signature 'GRangesList'
rescale(x, to = 1L, from = 1L)
```

Arguments

<code>x</code>	a <code>IRanges</code> , <code>GRanges</code> , <code>IRangesList</code> and <code>GRangesList</code> object
<code>to</code> , <code>from</code>	an <code>IRanges</code> object, a character vector coercible to <code>IRanges</code> or a integer vector parallel to <code>x</code> or with length = 1L.

Value

an object of the same type and dimensions as `x`

Author(s)

H. Pagès, F. Ernst

See Also

[IRanges](#) for details on character vectors coercible to `IRanges`.

Examples

```
x <- IRanges("5-10")
# widen the ranges
rescale(x, 100, 10)
# widen and shift
rescale(x, "31-60", "5-14")
```

`select`*Using the "select" interface on EpiTxDb objects*

Description

As expected for a `AnnotationDb` object, the general accessors `select`, `keys`, `columns` and `keytypes` can be used to get information from a [EpiTxDb](#) object.

Usage

```
## S4 method for signature 'EpiTxDb'
select(x, keys, columns, keytype, ...)

## S4 method for signature 'EpiTxDb'
columns(x)

## S4 method for signature 'EpiTxDb'
keys(x, keytype, ...)

## S4 method for signature 'EpiTxDb'
keytypes(x)
```

Arguments

`x` a [EpiTxDb](#) object
`keys`, `columns`, `keytype`, ...
See [AnnotationDb](#) for more comprehensive description of the methods `select`, `keys`, `columns` and `keytypes` and their arguments.

Value

a `data.frame` object for `select()` and a character vector for `keytypes()`, `keys()` and `columns()`.

Examples

```
etdb_file <- system.file("extdata", "EpiTxDb.Hs.hg38.snoRNAdb.sqlite",
                          package="EpiTxDb")
etdb <- loadDb(etdb_file)
etdb
```

`shiftTranscriptToGenomic`*Shift GRanges coordinates based on another GRanges object*

Description

`shiftGenomicToTranscript` shifts positions of a [GRanges](#) object based on coordinates of another [GRanges](#) object. The most common application is to shift genomic coordinates to transcript coordinates, which is reflected in the name. `shiftTranscriptToGenomic` implements the reverse operation.

Matches are determined by [findOverlaps](#) for `shiftGenomicToTranscript` and by [findMatches](#) for `shiftTranscriptToGenomic` using the seqnames of the subject and the names of tx.

Usage

```
shiftTranscriptToGenomic(subject, tx)

shiftGenomicToTranscript(subject, tx)

## S4 method for signature 'GRanges,GRangesList'
shiftTranscriptToGenomic(subject, tx)

## S4 method for signature 'GRangesList,GRangesList'
shiftTranscriptToGenomic(subject, tx)

## S4 method for signature 'GRanges,GRangesList'
shiftGenomicToTranscript(subject, tx)

## S4 method for signature 'GRangesList,GRangesList'
shiftGenomicToTranscript(subject, tx)
```

Arguments

<code>subject</code>	a GRanges or GRangesList object
<code>tx</code>	a named GRangesList object.

Value

a [GRanges](#) or [GRangesList](#) object depending on the type of subject

Examples

```
library(GenomicRanges)
# Construct some example data
subject1 <- GRanges("chr1", IRanges(3, 6),
                    strand = "+")
subject2 <- GRanges("chr1", IRanges(c(17,23), width=3),
```

```

strand = c("+","-"))
subject3 <- GRanges("chr2", IRanges(c(51, 54), c(53, 59)),
strand = "-")
subject <- GRangesList(a=subject1, b=subject2, c=subject3)
tx1 <- GRanges("chr1", IRanges(1, 40),
strand="+")
tx2 <- GRanges("chr1", IRanges(10, 30),
strand="+")
tx3 <- GRanges("chr2", IRanges(50, 60),
strand="-")
tx <- GRangesList(a=tx1, b=tx2, c=tx3)

# shift to transcript coordinates. Since the third subject does not have
# a match in tx it is dropped with a warning
shifted_grl <- shiftGenomicToTranscript(subject,tx)

# ... and back
shifted_grl2 <- shiftTranscriptToGenomic(shifted_grl,tx)

# comparison of ranges work. However the seqlevels differ
ranges(shifted_grl2) == ranges(subject[list(1,c(1,1),c(1,2))])

```

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