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.

**License**  Artistic-2.0

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

**Suggests**  BiocStyle, knitr, rmarkdown, testthat, httptest, AnnotationHub, ensembldb, ggplot2, EpiTxDb.Hs.hg38, BSgenome.Hsapiens.UCSC.hg38, BSgenome.Scerevisiae.UCSC.sacCer3, TxDb.Hsapiens.UCSC.hg38.knownGene

**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'

**RoxygenNote**  7.3.1

**BugReports**  https://github.com/FelixErnst/EpiTxDb/issues
EpiTxDb-package

EpiTxDb: Storing and accessing epitranscriptomic information using the AnnotationDbi interface

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)

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**EpiTxDb-class**

### See Also

Useful links:

- [https://github.com/FelixErnst/EpiTxDb](https://github.com/FelixErnst/EpiTxDb)
- Report bugs at [https://github.com/FelixErnst/EpiTxDb/issues](https://github.com/FelixErnst/EpiTxDb/issues)

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**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

```r
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
```

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**EpiTxDb-data**

**EpiTxDb internal data**

### Description

EpiTxDb internal data

### Usage

```r
data(rmbase_data)
```

### Format

```r
data.frame
```
Description

title

Author(s)

Felix G M Ernst [aut]

References


makeEpiTxDb

Creating a EpiTxDb from user supplied annotations as data.frames

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.
• spec_entrezid: a character or factor with an entrezid for the gene-
  name of the specifier.
  (default: specifiers = NULL)

references An optional data.frame containing the following columns:

  • mod_id: a integer value per modification and the link to the modification
    data.frame.
  • ref_type: a character or factor with a reference type, e.g. PMID. Is not
    checked for validity.
  • ref: a character or factor with a reference value, e.g. a specific pubmed
    id or an journal article. Is not checked for validity.
  (default: references = NULL)

metadata An optional data.frame containing the following columns:

  • name: a character value used as name
  • value: a character value

This dataframe will be returned by metadata() (default: metadata = NULL)

reassign.ids TRUE or FALSE Controls how internal mod_ids should be assigned. If reassign.ids
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,
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

```r
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)
```

Description

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

Usage

```r
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 removeIncompatibleModification
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 us-
ing 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.

Description

makeEpiTxDbFromtRNAdb will make use of the tRNAdb online resources and extract the modifica-
tion 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

```r
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


Examples

```r
## 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)
positionSequence 13

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)

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 Generate integer sequences from position information of Ranges

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

x a IRanges, GRanges, IRangesList and GRangesList object
to, from an IRanges object, a character vector coercible to IRanges or a integer vector parallel to x 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")
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

```r
## 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

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

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

subject a GRanges or GRangesList object

tx 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 = "+")
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 seqlvels differ
ranges(shifted_grl2) == ranges(subject[[list(1,c(1,1),c(1,2))]])
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