Package ‘EpiTxDb’

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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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R topics documented:

- EpiTxDb-package ........................................... 2
- EpiTxDb-class ........................................... 3
- EpiTxDb-data ........................................... 4
- makeEpiTxDb ........................................... 5
- makeEpiTxDbFromGRanges ................................... 7
- makeEpiTxDbFromRMBase ................................... 8
- makeEpiTxDbFromtRNAdb ................................... 10
- modifications ........................................... 11
- positionSequence ....................................... 13
- rescale .................................................. 14
- select .................................................. 15
- shiftTranscriptToGenomic ............................... 16

Index 18

EpiTxDb-package EpiTxDb - Storing and accessing epitranscriptomic information using the AnnotationDbi interface

Description

title

Author(s)

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EpiTxDb-class

References


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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**

```r
## 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**

- organism() and seqlevels() a character vector
- seqinfo() a Seqinfo object
- as.list() a list
See Also

- `makeEpiTxDbFromGRanges` for creating an EpiTxDb object from a `GRanges` object and its metadata columns
- `makeEpiTxDbFromRMBase` for creating an EpiTxDb object from RMBase online resources
- `makeEpiTxDbFromtRNAdb` for creating an EpiTxDb object from tRNAdb online resources
- `makeEpiTxDb` for creating an 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
```

---

**EpiTxDb-data**  
*EpiTxDb internal data*

**Description**

EpiTxDb internal data

**Usage**

```r
data(rmbase_data)
```

**Format**

```r
data.frame
```
**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 function typically will not be used by regular users.

**Usage**

```r
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`: an 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.
makeEpiTxDb

- `rx_rank`: an integer for sorting enzyme reactions, if multiple enzymes are involved in the modification’s incorporation/maintenance.
- `rx_ensemble`: a character or factor with an ensembl identifier for the genename of the enzyme.
- `rx_ensembletrans`: 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`: an 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_ensemble`: a character or factor with an ensembl identifier for the genename of the specifier.
- `spec_ensembletrans`: 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 genename of the specifier.

(default: `specifiers = NULL`)

`references`  An optional data.frame containing the following columns:
- `mod_id`: an 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_id`s 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 its 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

```r
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)
```

Description

`makeEpiTxDbFromGRanges` extracts information 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)
g <- GRanges(sequenames = "test",
ranges = IRanges::IRanges(1,1),
strand = "+",
Dataframe(mod_id = 1L,
  mod_type = "Am",
  mod_name = "Am_1"))
etdb <- makeEpiTxDbFromGRanges(g)
```

Description

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

Usage

    makeEpiTxDbFromRMBase(organism, genome, modtype)

    downloadRMBaseFiles(organism, genome, modtype)

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

getRMBaseDataAsGRanges(files)

makeEpiTxDbFromRMBaseFiles(
  files,
  tx = NULL,
  sequences = NULL,
  metadata = NULL,
  reassign.ids = 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

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.
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.
modifications

References


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)

- **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)
```

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)
```
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.
**select**

**Examples**

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

**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

*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**

```r
shiftTranscriptToGenomic(subject, tx)
shiftGenomicToTranscript(subject, tx)
```

### S4 method for signature 'GRanges,GRangesList'

```r
shiftTranscriptToGenomic(subject, tx)
```

### S4 method for signature 'GRangesList,GRangesList'

```r
shiftTranscriptToGenomic(subject, tx)
```

### S4 method for signature 'GRanges,GRangesList'

```r
shiftGenomicToTranscript(subject, tx)
```

### S4 method for signature 'GRangesList,GRangesList'

```r
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**

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

```r
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="+")

# 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))]])
```
Index

* datasets
  EpiTxDb-data, 4
  makeEpiTxDbFromRMBase, 8
  .EpiTxDb (EpiTxDb-class), 3
  ?combineIntoModstrings, 12
AnnotationDb, 3, 4, 15
as.integer, Ranges-method
  (positionSequence), 13
as.list, EpiTxDb-method
  (EpiTxDb-class), 3
BiocFileCache, 9

columns (select), 15
columns, EpiTxDb-method (select), 15
combineIntoModstrings(), 11, 12

DNAStringSet, 10
downloadRMBaseFiles
  (makeEpiTxDbFromRMBase), 8

EpiTxDb, 5, 11, 12, 15
EpiTxDb (EpiTxDb-class), 3
EpiTxDb-class, 3
EpiTxDb-data, 4
EpiTxDb-package, 2
EPIITXDB_RMBASE_URL
  (makeEpiTxDbFromRMBase), 8

findMatches, 16
findOverlaps, 16

getRMBaseDataAsGRanges
  (makeEpiTxDbFromRMBase), 8
gettRNAdbDataAsGRanges
  (makeEpiTxDbFromtRNAdb), 10

GRanges, 4, 7, 8, 12, 13, 16
GRangesList, 9, 12, 13, 16

import.tRNAdb, 10

IRanges, 13, 14
IRangesList, 13
keys (select), 15
keys, EpiTxDb-method (select), 15
keytypes (select), 15
keytypes, EpiTxDb-method (select), 15

listAvailableGenomesFromRMBase
  (makeEpiTxDbFromRMBase), 8
listAvailableModFromRMBase
  (makeEpiTxDbFromRMBase), 8
listAvailableOrganismsFromRMBase
  (makeEpiTxDbFromRMBase), 8
listAvailableOrganismsFromtRNAdb
  (makeEpiTxDbFromtRNAdb), 10

makeEpiTxDb, 4, 5, 7–10
makeEpiTxDbFromGRanges, 4, 7, 7
makeEpiTxDbFromRMBase, 4, 7, 8
makeEpiTxDbFromRMBaseFiles
  (makeEpiTxDbFromRMBase), 8
makeEpiTxDbFromtRNAdb, 4, 7, 10
modifications, 4, 11
modifications, EpiTxDb-method
  (modifications), 11
modificationsBy, 4
modificationsBy (modifications), 11
modificationsBy, EpiTxDb-method
  (modifications), 11

modifiedSeqsByTranscript
  (modifications), 11
modifiedSeqsByTranscript, EpiTxDb, DNAStringSet-method
  (modifications), 11

ModRNAString, 7
ModRNAStringSet, 11

organism, EpiTxDb-method
  (EpiTxDb-class), 3

positionSequence, 13
INDEX

positionSequence, Ranges-method (positionSequence), 13
positionSequence, RangesList-method (positionSequence), 13
removeIncompatibleModifications(), 9
rescale, 14
rescale, GRanges-method (rescale), 14
rescale, GRangesList-method (rescale), 14
rescale, IRanges-method (rescale), 14
rescale, IRangesList-method (rescale), 14
rmbase_data (EpiTxDb-data), 4
select, 4, 15
select, EpiTxDb-method (select), 15
Seqinfo, 3
seqinfo, EpiTxDb-method (EpiTxDb-class), 3
seqlevels, EpiTxDb-method (EpiTxDb-class), 3
shiftGenomicToTranscript, 4
shiftGenomicToTranscript (shiftTranscriptToGenomic), 16
shiftGenomicToTranscript, GRanges, GRangesList-method (shiftTranscriptToGenomic), 16
shiftGenomicToTranscript, GRangesList, GRangesList-method (shiftTranscriptToGenomic), 16
shiftTranscriptToGenomic, 4, 16
shiftTranscriptToGenomic, GRanges, GRangesList-method (shiftTranscriptToGenomic), 16
shiftTranscriptToGenomic, GRangesList, GRangesList-method (shiftTranscriptToGenomic), 16
shortName, 7
tRNAdbImport, 10