Package ‘transmogR’

May 30, 2024

Type  Package
Title  Modify a set of reference sequences using a set of variants
Version  1.0.0
Description  transmogR provides the tools needed to create a new reference genome or reference transcriptome, using a set of variants. Variants can be any combination of SNPs, Insertions and Deletions. The intended use-case is to enable creation of variant-modified reference transcriptomes for incorporation into transcriptomic pseudo-alignment workflows, such as salmon.

License  GPL-3
Encoding  UTF-8

URL  https://github.com/smped/transmogR

BugReports  https://github.com/smped/transmogR/issues

Depends  Biostrings, GenomicRanges

Imports  BSgenome, GenomeInfoDb, GenomicFeatures, ggplot2 (>= 3.5.0), IRanges, methods, parallel, rlang, scales, stats, S4Vectors, SummarizedExperiment, VariantAnnotation

Suggests  BiocStyle, BSgenome.Hsapiens.UCSC.hg38, ComplexUpset, extraChIPs, InteractionSet, knitr, rmarkdown, rtracklayer, testthat (>= 3.0.0)

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BiocType  Software

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transmogR-package

Description

The package transmogR has been designed for creation of a variant-modified reference transcriptome.

Details

The package transmogR provides two primary functions for modifying complete transcriptomes or genomes:

- `transmogrify()` for incorporating the supplied variants into transcriptomic sequences, and
- `genomogrify()` for incorporating the supplied variants into genomic sequences, ideally to be passed as decoy sequences to a tool such as salmon.

The main functions rely on lower-level functions such as:

- `owl()` which over-writes letters (i.e. SNPs) within a sequence, and
- `indelcator()` which incorporates InDels into an individual sequence

Additional utility functions are provided which allow characterisation and exploration of any set of variants:
• `overlapsByVar()` counts the variants which overlap sets of GenomicRanges, first splitting the variants into SNV, Insertions and Deletions
• `parY()` returns the pseudo-autosomal regions for a chosen genome build as a GenomicRanges object
• `upsetVarByCol()` produces an UpSet plot counting how many unique IDs are impacted by a set of variants. IDs can represent any column in the supplied ranges, such as `gene_id` or `transcript_id`
• `varTypes()` classifies a set of variants into SNV, Insertions of Deletions

**Author(s)**
Stevie Pederson

**See Also**
Useful links:
• [https://github.com/smped/transmogR](https://github.com/smped/transmogR)
• Report bugs at [https://github.com/smped/transmogR/issues](https://github.com/smped/transmogR/issues)

---

**Description**
Use a set of SNPS, insertions and deletions to modify a reference genome

**Usage**

```r
genomogrify(x, var, ...)
```

## S4 method for signature 'XStringSet,GRanges'

```r
genomogrify(
x, 
var, 
alt_col = "ALT", 
mask = GRanges(), 
tag = NULL, 
sep = ",", 
var_tags = FALSE, 
var_sep = ",", 
verbose = TRUE, 
...
)
```

## S4 method for signature 'BSgenome,GRanges'

```r
```
genomogrify(x, var, alt_col = "ALT", mask = GRanges(), names, tag = NULL, sep = "_", var_tags = FALSE, var_sep = "_", verbose = TRUE, ...)

## S4 method for signature 'BSgenome,VcfFile'

genomogrify(x, var, alt_col = "ALT", mask = GRanges(), names, tag = NULL, sep = "_", var_tags = FALSE, var_sep = "_", which, verbose = TRUE, ...)

## S4 method for signature 'XStringSet,VcfFile'

genomogrify(x, var, alt_col = "ALT", mask = GRanges(), tag = NULL, sep = "_", var_tags = FALSE, var_sep = "_", which, verbose = TRUE, ...)

Arguments

x A DNAStringSet or BSgenome
genomogrify

- `var` GRanges object containing the variants, or a VariantAnnotation::VcfFile
- `...` Passed to parallel::mclapply
- `alt_col` The name of the column with var containing alternate bases
- `mask` Optional GRanges object defining regions to be masked with an 'N'
- `tag` Optional tag to add to all sequence names which were modified
- `sep` Separator to place between seqnames names & tag
- `var_tags` logical(1) Add tags indicating which type of variant were incorporated, with 's', 'i' and 'd' representing SNPs, Insertions and Deletions respectively
- `var_sep` Separator between any previous tags and variant tags
- `verbose` logical(1) Print progress messages while running
- `names` Sequence names to be mogrified
- `which` GRanges object passed to VariantAnnotation::ScanVcfParam if using a VCF directly

Details

This function is designed to create a variant-modified reference genome, intended to be included as a set of decoys when using salmon in selective alignment mode. Sequence lengths will change if InDels are included and any coordinate-based information will be lost on the output of this function.

Tags are able to be added to any modified sequence to assist identifying any changes that have been made to a sequence.

Value

XStringSet with variant modified sequences

Examples

```r
library(GenomicRanges)
dna <- DNAStringSet(c(chr1 = "ACGT", chr2 = "AATTT"))
var <- GRanges(c("chr1:1", "chr1:3", "chr2:1-3"))
var$ALT <- c("C", "GG", "A")
dna
genomogrify(dna, var)
genomogrify(dna, var, tag = "mod")
genomogrify(dna, var, var_tags = TRUE)
genomogrify(dna, var, mask = GRanges("chr2:1-5"), var_tags = TRUE)
```
indelcator

Substitute InDels into one or more sequences

Description

Modify one or more sequences to include Insertions or Deletions

Usage

indelcator(x, indels, ...)

## S4 method for signature 'XString,GRanges'
indelcator(x, indels, exons, alt_col = "ALT", ...)

## S4 method for signature 'DNAStringSet,GRanges'
indelcator(x, indels, alt_col = "ALT", mc.cores = 1, verbose = TRUE, ...)

## S4 method for signature 'BSgenome,GRanges'
indelcator(x, indels, alt_col = "ALT", mc.cores = 1, names, ...)

Arguments

x  Sequence of class XString
indels  GRanges object with InDel locations and the alternate allele
...  Passed to parallel::mclapply
exons  GRanges object containing exon structure for x
alt_col  Column containing the alternate allele
mc.cores  Number of cores to use when calling parallel::mclapply internally
verbose  logical(1) Print all messages
names  passed to BSgenome::getSeq when x is a BSgenome object

Details

This is a lower-level function relied on by both transmogrify() and genomogrify().

Takes an Biostrings::XString or Biostrings::XStringSet object and modifies the sequence to incorporate InDels. The expected types of data determine the behaviour, with the following expectations describing how the function will incorporate data

<table>
<thead>
<tr>
<th>Input Data Type</th>
<th>Exons Required</th>
<th>Use Case</th>
<th>Returned</th>
</tr>
</thead>
<tbody>
<tr>
<td>XString</td>
<td>Y</td>
<td>Modify a Reference Transcriptome</td>
<td>XString</td>
</tr>
<tr>
<td>DNAStringSet</td>
<td>N</td>
<td>Modify a Reference Genome</td>
<td>DNAStringSet</td>
</tr>
<tr>
<td>BSgenome</td>
<td>N</td>
<td>Modify a Reference Genome</td>
<td>DNAStringSet</td>
</tr>
</tbody>
</table>
overlapsByVar

Value
A DNAStringSet or XString object (See Details)

See Also
transmogrify() genomogrify()

Examples

## Start with a DNAStringSet
library(GenomicRanges)
seq <- DNAStringSet(c(seq1 = "AATCTGCGC"))
## Define an Insertion
var <- GRanges("seq1:1")
var$ALT <- "AAA"
seq
indelcator(seq, var)

## To modify a single transcript
library(GenomicFeatures)
ex <- GRanges(c("seq1:1-3:+", "seq1:7-9:+"))
orig <- extractTranscriptSeqs(seq, GRangesList(tx1 = ex))[["tx1"]]
orig
indelcator(orig, var, exons = ex)

overlapsByVar Count overlaps by variant type

Description
Count how many variants of each type overlap ranges

Usage
overlapsByVar(x, var, ...)

## S4 method for signature 'GRangesList,GRanges'
overlapsByVar(x, var, alt_col = "ALT", ...)

## S4 method for signature 'GRanges,GRanges'
overlapsByVar(x, var, alt_col = "ALT", ...)

Arguments

x A GRangesList with features of interest
var A Granges object with variants of interest
... Passed to rowSums
alt_col The column within mcols(var) which contains the alternate allele
Details

Taking any GRanges or GRangesList, count how many of each variant type overlap a region.

Value

A vector or matrix

Examples

library(rtracklayer)
library(VariantAnnotation)

gtf <- import.gff(
  system.file("extdata/gencode.v44.subset.gtf.gz", package = "transmogR")
)
grl <- splitAsList(gtf, gtf$type)
vcf <- system.file("extdata/1000GP_subset.vcf.gz", package = "transmogR")
var <- rowRanges(readVcf(vcf, param = ScanVcfParam(fixed = "ALT")))
overlapsByVar(grl, var)

---

owl

OverWrite Letters in an XStringSet

Description

OverWrite Letters (e.g. SNPs) in an XStringSet

Usage

owl(seq, snps, ...)

## S4 method for signature 'XStringSet,GRanges'
owl(seq, snps, alt_col = "ALT", ...)

## S4 method for signature 'BSgenome,GRanges'
owl(seq, snps, alt_col = "ALT", names, ...)

Arguments

seq A BSgenome, DNAStringSet, RNAStringSet or other XStringSet.
snps A GRanges object with SNP positions and a column containing the alternate allele
... Passed to Biostrings::replaceLetterAt()
alt_col Column name in the mcols element of snps containing the alternate allele
names Sequence names to operate on
Details

This is a lower-level function called by `transmogrify()` and `genomogrify()`, but able to be called by the user if needed.

Note that when providing a BSgenome object, this will first be coerced to a DNAStringSet which can be time consuming.

Value

An object of the same class as the original object, but with SNPs inserted at the supplied positions.

Examples

```r
seq <- DNAStringSet(c(chr1 = "AAGC"))
snps <- GRanges("chr1:2")
snps$ALT <- "G"
seq
owl(seq, snps)
```

---

**parY**  
*Get the PAR-Y Regions From a Seqinfo Object*

Description

Define the Pseudo-Autosomal Regions from a Seqinfo Object.

Usage

```r
parY(x, ...)  
```

Arguments

- **x**  
  A Seqinfo object or any of named build. If passing a character vector, `match.arg()` will be used to match the build.

- **...**  
  Not used.

- **prefix**  
  Optional prefix to place before chromosome names. Can only be NULL, "" or "chr""
Details

Using a seqinfo object based on either hg38, hg19, CHM13.v2 or their variations, create a GRanges object with the Pseudo-Autosomal Regions from the Y chromosome for that build. The length of the Y chromosome on the seqinfo object is used to determine the correct genome build when passing a Seqinfo object. Otherwise, an additional mcols column called PAR will indicate PAR1 and PAR2.

Value

A GenomicRanges object

Examples

```r
library(GenomeInfoDb)
sq <- Seqinfo(
  seqnames = "chrY", seqlengths = 59373566, genome = "hg19_only_chrY"
)
parY(sq)

## PAR regions for CHM13 are also available
sq <- Seqinfo(
  seqnames = "chrY", seqlengths = 62460029, genome = "CHM13"
)
parY(sq)

## Or just call by name
parY("GRCh38", prefix = "chr")
```

sjFromExons

Obtain Splice-Junctions from Exons and Transcripts

Description

Using GRanges defining exons and transcripts, find the splice-junctions.

Usage

```r
sjFromExons(
  x,
  rank_col = c("exon_number", "exon_rank"),
  tx_col = c("transcript_id", "tx_id"),
  extra_cols = "all",
  don_len = 8,
  acc_len = 5,
  as = c("GRanges", "GInteractions"),
  ...
)
```
Arguments

- **x**: GRanges object with exons and transcripts. A column indicating the position (or rank) of each exon within the transcript must be included.
- **rank_col**: The column containing the position of each exons within the transcript
- **tx_col**: The column containing unique transcript-level identifiers
- **extra_cols**: Can be a vector of column names to return beyond rank_col and tx_col. By default all columns are returned (extra_cols = "all").
- **don_len, acc_len**: Length of donor and acceptor sites respectively
- **as**: Return as a set of GenomicRanges, or with each splice junction annotated as a GenomicInteraction
- **...**: Not used

Details

A canonical splice junction consists of a donor site and an acceptor site at each end of an intron, with a branching site somewhere within the intron. Canonical donor sites are 8nt long with the the first two bases being exonic and the next 6 being derived form intronic sequences. Canonical acceptor sites are 5nt long with the first four bases being intronic and the final base being the first base of the next exon.

This functions uses each set of exons within a transcript to identify both donor and acceptor sites. Branch sites are not identified.

Value

A GRanges object with requested columns, and an additional column, 'site', annotating each region as a donor or acceptor site.

Alternatively, by specifying as = "GInteractions", the junctions can be returned with each splice junction annotated as a GenomicInteraction. This can make the set of junctions easier to interpret for a given transcript.

Examples

```r
library(rtracklayer)
gtf_cols <- c(
  "transcript_id", "transcript_name", "gene_id", "gene_name", "exon_number"
)
gtf <- import.gff(
  system.file("extdata/gencode.v44.subset.gtf.gz", package = "transmogR"),
  feature.type = "exon", colnames = gtf_cols
)
sj <- sjFromExons(gtf)
sj

## Or to simplify shared splice junctions across multiple transcripts
library(extraChIPs, quietly = TRUE)
chopMC(sj)
```
transmogrify

Mogrify a transcriptome using a set of variants

Description

Use a set of SNPs, insertions and deletions to modify a reference transcriptome

Usage

transmogrify(x, var, exons, ...)

## S4 method for signature 'XStringSet,GRanges,GRanges'
transmogrify(
  x,
  var,
  exons,
  alt_col = "ALT",
  trans_col = "transcript_id",
  omit_ranges = NULL,
  tag = NULL,
  sep = "_",
  var_tags = FALSE,
  var_sep = "_",
  verbose = TRUE,
  mc.cores = 1,
  ...
)

## S4 method for signature 'BSgenome,GRanges,GRanges'
transmogrify(
  x,
  var,
  exons,
  alt_col = "ALT",
  trans_col = "transcript_id",
  omit_ranges = NULL,
  tag = NULL,
  sep = "_",
  var_tags = FALSE,
  var_sep = "_",
  verbose = TRUE,
mc.cores = 1,
...
)

## S4 method for signature 'BSgenome,VcfFile,GRanges'
transmogrify(
  x,
  var,
  exons,
  alt_col = "ALT",
  trans_col = "transcript_id",
  omit_ranges = NULL,
  tag = NULL,
  sep = ",",
  var_tags = FALSE,
  var_sep = ",",
  verbose = TRUE,
  mc.cores = 1,
  which,
  ...
)

## S4 method for signature 'XStringSet,VcfFile,GRanges'
transmogrify(
  x,
  var,
  exons,
  alt_col = "ALT",
  trans_col = "transcript_id",
  omit_ranges = NULL,
  tag = NULL,
  sep = ",",
  var_tags = FALSE,
  var_sep = ",",
  verbose = TRUE,
  mc.cores = 1,
  which,
  ...
)

Arguments

x Reference genome as either a DNAStringSet or BSgenome
var GRanges object containing the variants
exons GRanges object with ranges representing exons
... Passed to parallel::mclapply
alt_col Column from var containing alternate bases
transmogrify

trans_col Column from `exons` containing the transcript_id
omitted ranges GRanges object containing ranges to omit, such as PAR-Y regions, for example
tag Optional tag to add to all sequence names which were modified
sep Separator to place between seqnames names & tag
var_tags logical(1) Add tags indicating which type of variant were incorporated, with 's', 'i' and 'd' representing SNPs, Insertions and Deletions respectively
var_sep Separator between any previous tags and variant tags
verbose logical(1) Include informative messages, or operate silently
mc.cores Number of cores to be used when multi-threading via `parallel::mclapply`
which GRanges object passed to `VariantAnnotation::ScanVcfParam` if using a VCF directly

Details

Produce a set of variant modified transcript sequences from a standard reference genome. Supported variants are SNPs, Insertions and Deletions

Ranges needing to be masked, such as the Y-chromosome, or Y-PAR can be provided.

**It should be noted that this is a time consuming process** Inclusion of a large set of insertions and deletions across an entire transcriptome can involve individually modifying many thousands of transcripts, which can be a computationally demanding task. Whilst this can be parallelised using an appropriate number of cores, this may also prove taxing for lower power laptops, and pre-emptively closing memory hungry programs such as Slack, or internet browsers may be prudent.

Value

An XStringSet

Examples

```r
library(GenomicRanges)
library(GenomicFeatures)
seq <- DNAStringSet(c(chr1 = "ACGTAATGG"))
exons <- GRanges(c("chr1:1-3:-", "chr1:7-9:-"))
exons$transcript_id <- c("trans1")

# When using `extractTranscriptSeqs` -stranded exons need to be sorted by end
exons <- sort(exons, decreasing = TRUE, by = ~end)

trByExon <- splitAsList(exons, exons$transcript_id)

# Check the sequences
seq
extractTranscriptSeqs(seq, trByExon)

# Define some variants
var <- GRanges(c("chr1:2", "chr1:8"))
var$ALT <- c("A", "GGG")
```
upsetVarByCol

# Include the variants adding tags to indicate a SNP and indel
# The exons GRanges object will be split by transcript internally
transmogrify(seq, var, exons, var_tags = TRUE)

upsetVarByCol  Show Variants by Impacted Columns

Description

Produce an UpSet plot showing unique values from a given column

Usage

upsetVarByCol(
  gr,
  var,
  alt_col = "ALT",
  mcol = "transcript_id",
  ...
  intersection_args = list(),
  intersection_lab = "Intersection Size",
  set_geom = geom_bar(width = 0.6),
  set_expand = 0.2,
  set_counts = TRUE,
  hjust_counts = 1.1,
  set_lab = "Set Size",
  title
)

Arguments

gr  GRanges object with ranges representing a key feature such as exons
var  GRanges object with variants in a given column
alt_col  Column within var containing the alternate allele
mcol  The column within gr to summarise results by
...  Passed to ComplexUpset::upset
intersection_args
  See ComplexUpset::intersection_size for possible values
intersection_lab  Y-axis label for the intersection panel
set_geom  Passed to ComplexUpset::upset_set_size
set_expand  Expand the set-size axis by this amount
set_counts  logical(1) Show counts on set sizes
Identify SNVs, Insertions and Deletions

Identify SNVs, Insertions and Deletions within a GRanges object

Usage

`varTypes(x, alt_col = "ALT", ...)`

Arguments

- `x` GenomicRanges object
- `alt_col` Name of the column with mcols(x) which contains the alternate allele. Can be an XStringSetList, XStringSet or character
- `...` Not used
Details

Using the width of the reference and alternate alleles, classify each range as an SNV, Insertion or Deletion.

- SNVs are expected to have REF & ALT widths of 1
- Insertions are expected to have ALT longer than REF
- Deletions are expected to have ALT shorter than REF

These are relatively permissive criteria

Value

Character vector

Examples

# Load the example VCF and classify ranges
library(VariantAnnotation)
f <- system.file("extdata/1000GP_subset.vcf.gz", package = "transmogR")
vcf <- readVcf(f)
gr <- rowRanges(vcf)
type <- varTypes(gr)
table(type)
gr[type != "SNV"]
Index

* internal
  transmogR-package, 2
Biostrings::replaceLetterAt(), 8
Biostrings::XString, 6
Biostrings::XStringSet, 6
BSgenome::getSeq, 6
ComplexUpset::intersection.size, 15
ComplexUpset::upset, 15, 16
ComplexUpset::upset.set.size, 15

génomogrify, 3
génomogrify(), 2, 6, 7, 9
génomogrify, BSgenome, GRanges-method (génomogrify), 3
génomogrify, BSgenome, VcfFile-method (génomogrify), 3
génomogrify, XStringSet, GRanges-method (génomogrify), 3
génomogrify, XStringSet, VcfFile-method (génomogrify), 3
génomogrify-methods (génomogrify), 3

indelocator, 6
indelocator(), 2
indelocator, BSgenome, GRanges-method (indelocator), 6
indelocator, DNAStringSet, GRanges-method (indelocator), 6
indelocator, XString, GRanges-method (indelocator), 6

match.arg(), 9

overlapsByVar, 7
overlapsByVar(), 3
overlapsByVar, GRanges, GRanges-method (overlapsByVar), 7
overlapsByVar, GRangesList, GRanges-method (overlapsByVar), 7
overlapsByVar-methods (overlapsByVar), 7
owl, 8
owl(), 2
owl, BSgenome, GRanges-method (owl), 8
owl, XStringSet, GRanges-method (owl), 8
parallel::mclapply, 5, 6, 13, 14
parY, 9
parY(), 3
parY, character-method (parY), 9
parY, Seqinfo-method (parY), 9
parY-methods (parY), 9
rowSums, 7

sjFromExons, 10

transmogr (transmogR-package), 2
transmogR-package, 2
transmogrify, 12
transmogrify(), 2, 6, 7, 9
transmogrify, BSgenome, GRanges, GRanges-method (transmogrify), 12
transmogrify, BSgenome, VcfFile, GRanges-method (transmogrify), 12
transmogrify, XStringSet, GRanges, GRanges-method (transmogrify), 12
transmogrify, XStringSet, VcfFile, GRanges-method (transmogrify), 12
transmogrify-methods (transmogrify), 12

upsetVarByCol, 15
upsetVarByCol(), 3

VariantAnnotation:: ScanVcfParam, 5, 14
VariantAnnotation:: VcfFile, 5
varTypes, 16
varTypes(), 3