Package: transmogR (via r-universe)

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Type Package

Title Modify a set of reference sequences using a set of variants

Version 1.1.0

Description transmogR provides the tools needed to crate 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.

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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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Contents

`genomogrify` *Mogrify a genome using a set of variants*

Description

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

Usage

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

## S4 method for signature 'XStringSet,GRanges'
genomogrify(
  x,
  var,
  alt_col = "ALT",
  mask = GRanges(),
  tag = NULL,
  sep = "_",
  var_tags = FALSE,
  var_sep = "_",
  verbose = TRUE,
  ...
)

## S4 method for signature 'BSgenome,GRanges'
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
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

```
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

Input Data Type	Exons Required	Use Case	Returned
XString	Y	Modify a Reference Transcriptome	XString
DNAStringSet	N	Modify a Reference Genome	DNAStringSet
BSgenome	N	Modify a Reference Genome	DNAStringSet

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

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

```
parY(x, ...)

## S4 method for signature 'Seqinfo'
parY(x, ...)

## S4 method for signature 'character'
parY(x, prefix = NULL, ...)
```

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

```
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

```
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 wthin 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

```
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)

## Splice Junctions can also be returned as a GInteractions object with
## anchorOne as the donor & anchorTwo as the acceptor sites
sjFromExons(gtf, as = "GInteractions")
```

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
trans_col	Column from 'exons' containing the transcript_id
omit_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 browers may be prudent.

Value

An XStringSet

Examples

```
library(GenomicRanges)
library(GenomicFeatures)
seq <- DNAStringSet(c(chr1 = "ACGTAAATGG"))
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)
exons
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")

# 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
hjust_counts	Horizontal adjustment of counts, if being shown
set_lab	X-axis label for the set-sizes panel
title	Summary title to show above the intersection panel. Can be hidden by setting to NULL

Details

Take a set of variants, classify them as SNV, Insertion and Deletion, then using a GRanges object, produce an UpSet plot showing impacted values from a given column

Value

An UpSet plot

See Also

ComplexUpset::upset

Examples

```
library(rtracklayer)
library(VariantAnnotation)
gtf <- import.gff(
    system.file("extdata/gencode.v44.subset.gtf.gz", package = "transmogR"),
    feature.type = "exon"
)
vcf <- system.file("extdata/1000GP_subset.vcf.gz", package = "transmogR")
var <- rowRanges(readVcf(vcf, param = ScanVcfParam(fixed = "ALT")))
upsetVarByCol(gtf, var)
```

---

varTypes *Identify SNVs, Insertions and Deletions*

Description

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"]
```

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