

# *GenomicRanges* for Data and Annotation

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# Introduction

Importance of range concepts: conceptually...

- ▶ Genomic data and annotation can be represented by ranges
- ▶ Biological questions reflect range-based queries

Examples

- ▶ How many reads overlap each gene?
- ▶ How many reads span splice junctions?
- ▶ Where do regulatory elements bind in ChIP-seq experiments?
- ▶ Which regulatory elements are closest to differentially expressed genes?
- ▶ What sequences are common under discovered regulatory marks?

# Where do *GRanges*-like objects come from?

## Data

- ▶ From BAM files via `readGAlignments` in *GenomicAlignments*
- ▶ From BED files via `import` in *rtracklayer*

## Annotation

- ▶ *rtracklayer* `import` BED, WIG, GTF, ... files
- ▶ *TxDb.\** model organism gene models; *GenomicFeatures* `makeTranscriptDbFrom*`
- ▶ *AnnotationHub* – pre-computed instances from large public resources (later in course)

## Key reference

Lawrence et al., 2013, Software for Computing and Annotating Genomic Ranges. PLoS Comput Biol 9(8): e1003118<sup>2</sup>

- ▶ Initial developers: Michael Lawrence, Hervé Pagès, Patrick Aboyoun

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<sup>2</sup><http://www.ploscompbiol.org/article/info%3Adoi%2F10.1371%2Fjournal.pcbi.1003118>

# Ranges

What is a range?

- ▶ 'start' and 'end' coordinate vectors
- ▶ Closed interval (i.e., include end points)
- ▶ Zero-width convention
- ▶ Can be 'named'

```
library(IRanges)
eg <- IRanges(start= c(1, 10, 20),
              end  = c(4, 10, 19),
              names= c("A", "B", "C"))

## bigger
start <- floor(runif(10000, 1, 1000))
end   <- start + floor(runif(10000, 0, 100))
ir    <- IRanges(start, end)
```

# 'Accessors' and simple manipulation

## Accessors

- ▶ start, end, width, names

## 'Vector'-like behavior

- ▶ length, [

```
length(ir)
```

```
## [1] 10000
```

```
ir[1:4]
```

```
## IRanges of length 4
```

```
##      start end width
```

```
## [1]   871 921   51
```

```
## [2]   932 975   44
```

```
## [3]   916 937   22
```

```
## [4]   181 224   44
```

```
start(ir[1:4])
```

# Operations

1. Intra-range: operate on each range independently, e.g., `shift`
2. Inter-range: operate on several ranges of a single instance, e.g., `reduce`, `coverage`
3. Between-range: operate on two instances, e.g., `findOverlaps`

See table in afternoon lab!

```
ir <- IRanges(start=c(7, 9, 12, 14, 22:24),
              end=c(15, 11, 12, 18, 26, 27, 28))
shift(ir, 1)
```

```
## IRanges of length 7
```

```
##      start end width
```

```
## [1]      8  16     9
```

```
## [2]     10  12     3
```

```
## [3]     13  13     1
```

```
## [4]     15  19     5
```

```
## [5]     23  27     5
```

```
## [6]     24  28     5
```

```
## [7]     25  26     2
```

## *IRangesList*

- ▶ Often useful to group *IRanges* into a list, with each element of the list containing 0 or more *IRanges* instances
- ▶ Operations usually work on list element

```
irl <- split(ir, width(ir))  
reduce(irl)
```

```
## IRangesList of length 4
```

```
## $`1`
```

```
## IRanges of length 1
```

```
##      start end width
```

```
## [1]      12  12     1
```

```
##
```

```
## $`3`
```

```
## IRanges of length 1
```

```
##      start end width
```

```
## [1]       9  11     3
```

```
##
```



# GRanges

Builds on *IRanges*, *IRangesList*...

- ▶ 'seqnames' (e.g., chromosome) and 'strand'
- ▶ (optional) 'seqlengths' for genome information
- ▶ (optional) 'mcols' for 'metadata' data frame on each range

```
library(GenomicRanges)
genes <- GRanges(seqnames=c("chr3R", "chrX"),
  ranges=IRanges(
    start=c(19967117, 18962306),
    end  =c(19973212, 18962925),
    names=c("FBgn0039155", "FBgn0085359")),
  strand=c("+", "-"),
  seqlengths=c(chr3R=27905053L, chrX=22422827L))
mcols(genes) <-
  DataFrame(EntrezId=c("42865", "2768869"),
    Symbol=c("kal-1", "CG34330"))
```

# Coordinates and accessors

## Genome coordinates

- ▶ 1-based
- ▶ 'left-most' – 'start' of ranges on the minus strand are the left-most coordinate, rather than the 5' coordinate.

## Accessors

- ▶ `seqnames`, `strand`, `seqlengths`, `seqlevels` and like *IRanges*:  
`start`, `end`, `width`, `names`
- ▶ `mcols`; `$` for direct access to metadata

```
width(genes)
```

```
## [1] 6096 620
```

```
genes$Symbol
```

```
## [1] "kal-1" "CG34330"
```

## Operations

- ▶ Like *IRanges*, but generally seqnames- and strand-aware
- ▶ E.g., `flank` identifies *upstream* (5') region
- ▶ E.g., `findOverlaps` checks seqnames and strand

```
flank(genes, 1000) ## 5' flanking range
```

```
## GRanges with 2 ranges and 2 metadata columns:
```

```
##           seqnames           ranges strand |
##           <Rle>           <IRanges> <Rle> | <ch
##   FBgn0039155   chr3R [19966117, 19967116]   + |
##   FBgn0085359   chrX [18962926, 18963925]   - |
##           Symbol
##           <character>
##   FBgn0039155       kal-1
##   FBgn0085359       CG34330
##   ---
##   seqlengths:
##           chr3R       chrX
```

## \*List classes

- ▶ Often useful to have a list, where all elements of the list are restricted to be of the same type – like *IRangesList*
- ▶ Support for common 'atomic' types (*LogicalList*, *IntegerList*, *NumericList*, *CharacterList*, ...) in addition to *IRangesList*, *GRangesList*, ...
- ▶ Operations on list elements usually vectorized across elements

```
rl <- splitAsList(1:5, c("A", "B", "A", "B", "B"))  
elementLengths(rl)
```

```
## A B  
## 2 3
```

```
log(rl)
```

```
## NumericList of length 2  
## [["A"]] 0 1.09861228866811  
## [["B"]] 0.693147180559945 1.38629436111989 1.60943791243
```

## Three advanced concepts

1. *GRanges* extends *IRanges::Vector*, from which it inherits vector-like operations and metadata.
2. *\*List* data structures are actually vectors + a partitioning, so operations like `unlist`, `relist` and `split` are fast.
3. Many computationally expensive operations, e.g., `findOverlaps` are implemented in C, and are fast.