INTRODUCTION TO BIOCONDUCTOR

Sequence Ranges

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IRanges with numeric arguments

```
# Loading IRanges
library(IRanges)
```

A range is defined by `start` and `end`

```
myIRanges <- IRanges(start = 20, end = 30)
myIRanges
```

```
 IRanges object with 1 range and 0 metadata columns:
   start       end     width
<integer> <integer> <integer>
[1]        20        30        11
```

More IRanges examples

```
(myIRanges_width <- IRanges(start = c(1, 20), width = c(30, 11)))
```

```
 IRanges object with 2 ranges and 0 metadata columns:
         start       end     width
     <integer> <integer> <integer>
[1]         1        30        30
[2]        20        30        11
```

```
(myIRanges_end <- IRanges(start = c(1, 20), end = 30))
```

```
 IRanges object with 2 ranges and 0 metadata columns:
         start       end     width
     <integer> <integer> <integer>
[1]         1        30        30
[2]        20        30        11
```

Equation: `width = end - start + 1`

Rle - run length encoding

- Rle stands for Run length encoding
- Computes and stores the **lengths** and **values** of a vector or factor
- Rle is general S4 container used to save long repetitive vectors efficiently

```
(some_numbers <- c(3, 2, 2, 2, 3, 3, 4, 2))
[1] 3 2 2 2 3 3 4 2
```

```
(Rle(some_numbers))
numeric-Rle of length 8 with 5 runs
Lengths: 1 3 2 1 1
Values : 3 2 3 4 2
```

IRanges with logical vector

```
IRanges(start = c(FALSE, FALSE, TRUE, TRUE))
```

```
 IRanges object with 1 range and 0 metadata columns:
      start       end     width
  <integer> <integer> <integer>
[1]         3         4         2
```

IRanges with logical Rle

```
gi <- c(TRUE, TRUE, FALSE, FALSE, TRUE, TRUE, TRUE)

myRle <- Rle(gi)
```

```
logical-Rle of length 7 with 3 runs
Lengths:     2     2     3
Values :  TRUE FALSE  TRUE
```

```
IRanges(start = myRle)
```

```
IRanges object with 2 ranges and 0 metadata columns:
         start       end     width
      <integer> <integer> <integer>
[1]         1         2         2
[2]         5         7         3
```

In summary

IRanges are hierarchical data structures can contain metadata.

To construct IRanges objects:

- `start`, `end`, or `width` as numeric vectors (or NULL).
- `start` argument as a logical vector or logical Rle object.
  - Rle stands for Run length encoding and is storage efficient.
  - IRanges arguments get recycled (fill in the blanks).
  - equation for sequence range: `width = end - start + 1`.

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Let's practice using sequence ranges!

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Gene of interest using Genomic Ranges

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Examples of genomic intervals

- Reads aligned to a reference
- Genes of interest
- Exonic regions
- Single nucleotide polymorphisms (SNPs)
- Regions of transcription or binding sites, RNA-seq or ChIP-seq

Genomic Ranges

```
library(GenomicRanges)

(myGR <- GRanges("chr1:200-300"))
```

```
 GRanges object with 1 range and 0 metadata columns:
  seqnames     ranges strand
     <Rle>  <IRanges>  <Rle>
[1]     chr1 [200, 300]    *
-------
seqinfo: 1 sequence from an unspecified genome; no seqlengths
```

- GRanges class is a container to save genomic intervals by chromosome
- Minimum arguments `chr1:200-300`
- GRanges `seqnames` and `seqinfo`

From data to GRanges

```
# df a data.frame like structure
   seqnames start end strand score  GC
1      chrX    50 120      +     1 0.25
2      chrX   130 140      +     2 0.25
3      chrX   153 154      +     3 0.25
4      chrY    30  40      *     4 0.25
5      chrY    50  55      -     5 0.25
```

```
(myGR <- as(df, "GRanges")) # transform df into GRanges
```

```
GRanges object with 5 ranges and 2 metadata columns:
      seqnames     ranges strand |     score        GC
         <Rle>  <IRanges>  <Rle> | <integer> <numeric>
  [1]     chrX [ 50, 120]      + |         1      0.25
  [2]     chrX [130, 140]      + |         2      0.25
  [3]     chrX [153, 154]      + |         3      0.25
  [4]     chrY [ 30,  40]      * |         4      0.25
  [5]     chrY [ 50,  55]      - |         5      0.25
-------
 seqinfo: 2 sequences from an unspecified genome; no seqlengths
```

Genomic Ranges accessors

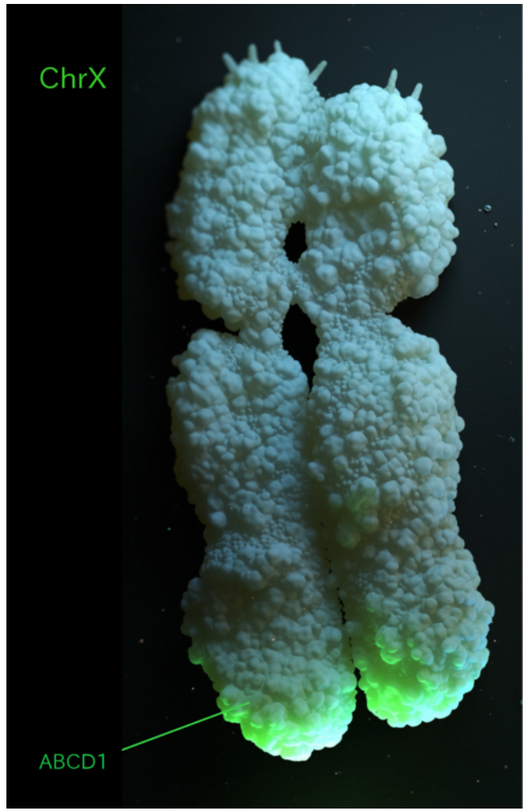
```
methods(class = "GRanges") # to check available accessors

# used for chromosome names
seqnames(gr)

# returns an IRanges object for ranges
ranges(gr)

# stores metadata columns
mcols(gr)

# generic function to store sequence information
seqinfo(gr)

# stores the genome name
genome(gr)
```

- Accessors are both setter and getter functions
- Accessors can be inherited thanks to S4 definitions

Gene of interest: ABCD1

- ABCD1 is located at the end of chromosome X long arm
- encodes a protein relevant for the well functioning of brain and lung cells in mammals
- chrX is ~ 156 mi bp
- Located chrX ~153.70 mi bp

https://www.ncbi.nlm.nih.gov/gene/215



Chromosome X GRanges

```
library(TxDb.Hsapiens.UCSC.hg38.knownGene)
hg <- TxDb.Hsapiens.UCSC.hg38.knownGene
```

Select genes from chromosome X

```
hg_chrXg <- genes(hg, filter = list(tx_chrom = c("chrX")))
```

```
GRanges object with 983 ranges and 1 metadata column:
          seqnames                ranges strand |     gene_id
             <Rle>             <IRanges>  <Rle> | <character>
    55344     chrX     [ 276322,  303356]      + |       55344
     6473     chrX     [ 624344,  659411]      + |        6473
     1438     chrX     [1268800, 1310381]      + |        1438
      ...      ...                    ...    ... .         ...
```

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Let's practice looking for a gene of interest in the human genome!

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Manipulating collections of GRanges

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GRangesList

- The `GRangesList-class` is a container for storing a collection of `GRanges`
  - Efficient for storing a large number of elements.
- To construct a `GRangesList`
  - `as(mylist, "GRangesList")`
  - `GRangesList(myGranges1, myGRanges2, ...)`
- To convert back to `GRanges`
  - `unlist(myGRangesList)`
- Accessors `methods(class = "GRangesList")`

When to use lists?

- Multiple GRanges objects may be combined into a GRangesList
  - GRanges in a list will be taken as compound features of a larger object
- Examples of GRangesLists are
  - transcripts by gene
  - exons by transcripts
  - read alignments
  - sliding windows

Break a region into smaller regions

```
# GRanges object with 983 genes
hg_chrX
```

```
slidingWindows(hg_chrX, width = 20000, step = 10000)
```

```
# showing only two elements of the list
GRangesList object of length 983:
[[1]]
GRanges object with 2 ranges and 0 metadata columns:
       seqnames           ranges strand
         <Rle>        <IRanges>  <Rle>
  [1]     chrX [276322, 296321]      +
  [2]     chrX [286322, 303356]      +
[[2]]
GRanges object with 3 ranges and 0 metadata columns:
       seqnames           ranges strand
  [1]     chrX [624344, 644343]      +
  [2]     chrX [634344, 654343]      +
  [3]     chrX [644344, 659411]      +
...
```

Genomic features and TxDb

`GenomicFeatures` uses transcript database (`TxDb`) objects to **store metadata, manage genomic locations and relationships between features and its identifiers**.

```
library(TxDb.Hsapiens.UCSC.hg38.knownGene)
(hg <- TxDb.Hsapiens.UCSC.hg38.knownGene)
```

```
Db type: TxDb
Supporting package: GenomicFeatures
Data source: UCSC
Genome: hg38
Organism: Homo sapiens
Taxonomy ID: 9606
Resource URL: http://genome.ucsc.edu/
Type of Gene ID: Entrez Gene ID
transcript_nrow: 197782
exon_nrow: 581036
cds_nrow: 293052
Db created by: GenomicFeatures package from Bioconductor
Creation time: 2016-09-29 13:02:09 +0000 (Thu, 29 Sep 2016)
```

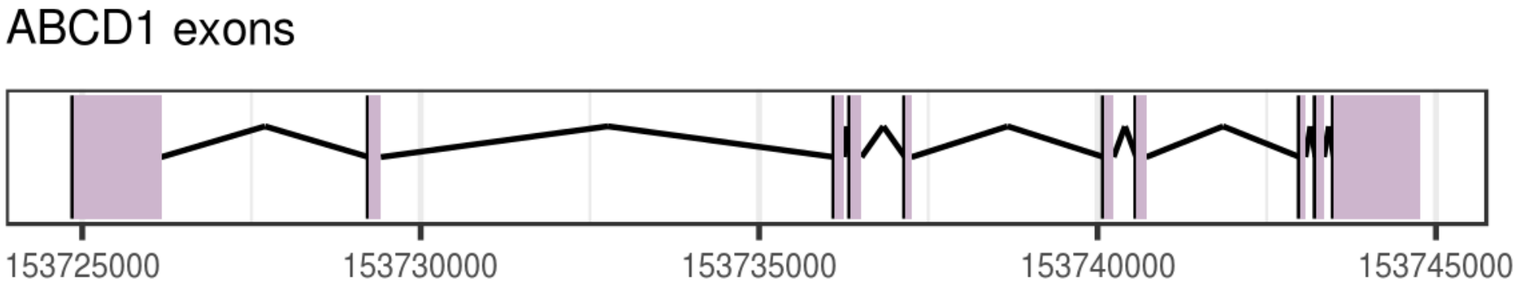
Genes, transcripts, exons

```
library(TxDb.Hsapiens.UCSC.hg38.knownGene)
hg <- TxDb.Hsapiens.UCSC.hg38.knownGene  #  hg is a A TxDb object

seqlevels(hg) <- c("chrX")               #  prefilter results to chrX

# transcripts
transcripts(hg, columns = c("tx_id", "tx_name"), filter = NULL)

# exons
exons(hg, columns = c("tx_id", "exon_id"), filter = list(tx_id = "179161"))
```

`columns` and `filter` can be NULL or any of these:

```
"gene_id", "tx_id", "tx_name", "tx_chrom", "tx_strand",
"exon_id", "exon_name", "exon_chrom", "exon_strand",
"cds_id", "cds_name", "cds_chrom", "cds_strand" and "exon_rank"
```

Exons by transcripts




```
hg <- TxDb.Hsapiens.UCSC.hg38.knownGene
seqlevels(hg) <- c("chrX")  #  prefilter chromosome X
exonsBytx <- exonsBy(hg, by = "tx")  #  exons by transcript

abcd1_179161 <- exonsBytx[["179161"]]  #  transcript id
```

```
width(abcd1_179161) # width of each exon, the purple regions of the figure

[1] 1299  181  143  169   95  146  146   85  126 1274
```

Overlaps

```
# countOverlaps results in an integer vector of counts
countOverlaps(query, subject)

# findOverlaps results in a Hits object
findOverlaps(query, subject)

# subsetByOverlaps returns a GRangesList object
subsetByOverlaps(query, subject)
```

- Query and subject are either a GRanges or GRangesList objects.
- Overlaps might be complete all partial.

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It's your turn to put this into practice!