

# Bioconductor Basics: Granges and Biostrings

- Core Bioconductor structures for representing genes and genetic sequences

## Motivation and Introduction

- Case study: given genomic DNA extracted from human cells, where on the genome does the nuclear protein ESRRA (estrogen related receptor alpha) bind?
- Role of estrogen receptors in breast cancer
- Data comes from analysis of ChIP-seq experiments: performed in ENCODE project - import info for files in “narrowPeak” format and analyze in Bioconductor GRanges object
- Identifying nearest transcriptional start site for each binding peak - assess whether regulatory activity of ESRRA occurs in transcriptional promoter regions

```
library(ERBS)
data(HepG2)
class(HepG2)
```

```
## [1] "GRanges"
## attr(,"package")
## [1] "GenomicRanges"
```

## GenomicRanges

- ERBS library from github repo
- Load two datasets - GM12878, HepG2. Estrogen receptor binding site datasets from two cell lines (cell-type dependent outcome).
- Contains: Chromosome start + end (1 row / region), strand information, score from peaks
- Access the GRanges objects as a matrix, i.e. subsetting is okay.
- **seqnames** function to access chromosome for each row. Returns object of type *Rle* - more efficient to save ordered by chromosome with counts. Can turn into character using **as.character**
- Most of analysis is focused on first 23 chromosomes
- Function to order by genomic region
- Iranges function not specific to genomics - Granges builds on Iranges in relation to genomics

```
# install ERBS
library(devtools)
```

```
## Loading required package: usethis
```

```
install_github("genomicsclass/ERBS")
```

```
## Skipping install of 'ERBS' from a github remote, the SHA1 (9f16eb6a) has not changed since last install.
## Use `force = TRUE` to force installation
```

```
library(GenomicRanges)
```

```
## Loading required package: stats4
```

```
## Loading required package: BiocGenerics
```

```
## Loading required package: parallel
```

```
##
```

```
## Attaching package: 'BiocGenerics'
```

```

## The following objects are masked from 'package:parallel':
##
##   clusterApply, clusterApplyLB, clusterCall, clusterEvalQ,
##   clusterExport, clusterMap, parApply, parCapply, parLapply,
##   parLapplyLB, parRapply, parSapply, parSapplyLB
## The following objects are masked from 'package:stats':
##
##   IQR, mad, sd, var, xtabs
## The following objects are masked from 'package:base':
##
##   anyDuplicated, append, as.data.frame, basename, cbind, colnames,
##   dirname, do.call, duplicated, eval, evalq, Filter, Find, get, grep,
##   grepl, intersect, is.unsorted, lapply, Map, mapply, match, mget,
##   order, paste, pmax, pmax.int, pmin, pmin.int, Position, rank,
##   rbind, Reduce, rownames, sapply, setdiff, sort, table, tapply,
##   union, unique, unsplit, which.max, which.min
## Loading required package: S4Vectors
##
## Attaching package: 'S4Vectors'
## The following object is masked from 'package:base':
##
##   expand.grid
## Loading required package: IRanges
## Loading required package: GenomeInfoDb
## Warning: package 'GenomeInfoDb' was built under R version 4.0.4
# load GM12878 and HepG2 objects from ERBS package
library(ERBS)
data(GM12878)
data(HepG2)

# inspect HepG2 GRanges object
class(HepG2)

## [1] "GRanges"
## attr(,"package")
## [1] "GenomicRanges"

HepG2

## GRanges object with 303 ranges and 7 metadata columns:
##      seqnames      ranges strand |      name      score      col
##      <Rle>         <IRanges> <Rle> | <numeric> <integer> <logical>
## [1]   chr2    20335378-20335787   * |      NA          0      <NA>
## [2]  chr20     328285-329145     * |      NA          0      <NA>
## [3]   chr6 168135432-168136587   * |      NA          0      <NA>
## [4]  chr19    1244419-1245304     * |      NA          0      <NA>
## [5]  chr11    64071828-64073069   * |      NA          0      <NA>
## ...      ...      ...      ... | ...      ...      ...
## [299] chr4      1797182-1797852     * |      NA          0      <NA>
## [300] chr1 110198573-110199126     * |      NA          0      <NA>
## [301] chr17   17734052-17734469     * |      NA          0      <NA>

```

```
## [302] chr1 48306453-48306908 * | NA 0 <NA>
## [303] chr12 123867207-123867554 * | NA 0 <NA>
##      signalValue    pValue      qValue      peak
##      <numeric> <numeric> <numeric> <integer>
## [1]      58.251      75.899 6.14371e-72      195
## [2]      10.808      69.685 5.02806e-66      321
## [3]      17.103      54.311 7.93067e-51      930
## [4]      12.427      43.855 1.35976e-40      604
## [5]      10.850      40.977 7.33386e-38      492
## ...      ...      ...      ...
## [299]      9.681      10.057 1.42334e-08      402
## [300]      7.929      10.047 1.44208e-08      197
## [301]      5.864      9.990 1.63892e-08      227
## [302]      5.660      9.948 1.79941e-08      211
## [303]     13.211      9.918 1.92180e-08      163
## -----
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
values(HepG2)
```

```
## DataFrame with 303 rows and 7 columns
##      name      score      col signalValue    pValue      qValue      peak
##      <numeric> <integer> <logical> <numeric> <numeric> <numeric> <integer>
## 1      NA          0      NA      58.251      75.899 6.14371e-72      195
## 2      NA          0      NA      10.808      69.685 5.02806e-66      321
## 3      NA          0      NA      17.103      54.311 7.93067e-51      930
## 4      NA          0      NA      12.427      43.855 1.35976e-40      604
## 5      NA          0      NA      10.850      40.977 7.33386e-38      492
## ...      ...      ...      ...      ...      ...      ...
## 299     NA          0      NA      9.681      10.057 1.42334e-08      402
## 300     NA          0      NA      7.929      10.047 1.44208e-08      197
## 301     NA          0      NA      5.864      9.990 1.63892e-08      227
## 302     NA          0      NA      5.660      9.948 1.79941e-08      211
## 303     NA          0      NA     13.211      9.918 1.92180e-08      163
```

```
# seqnames extracts chromosome names
seqnames(HepG2)      # stored as type Rle
```

```
## factor-Rle of length 303 with 292 runs
## Lengths:      1      1      1      1      1 ...      1      1      1      1      1
## Values : chr2 chr20 chr6 chr19 chr11 ... chr4 chr1 chr17 chr1 chr12
## Levels(93): chr1 chr2 chr3 ... chrUn_gl000247 chrUn_gl000248 chrUn_gl000249
```

```
chr = seqnames(HepG2)
as.character(chr)      # view as character type
```

```
## [1] "chr2" "chr20" "chr6" "chr19" "chr11" "chr20" "chr19" "chr2" "chr16"
## [10] "chr3" "chr6" "chr20" "chr7" "chr16" "chr9" "chr11" "chr22" "chrX"
## [19] "chr8" "chr16" "chr16" "chr19" "chr17" "chr17" "chr16" "chr1" "chr16"
## [28] "chr9" "chr17" "chr16" "chr12" "chr6" "chr2" "chr3" "chr11" "chr16"
## [37] "chr6" "chr2" "chr8" "chr1" "chr17" "chr20" "chr4" "chr14" "chr19"
## [46] "chr20" "chr9" "chr2" "chr2" "chr19" "chr8" "chr14" "chr22" "chr2"
## [55] "chr14" "chr6" "chr20" "chr2" "chr19" "chr8" "chr2" "chr19" "chr12"
## [64] "chr2" "chr2" "chr11" "chr12" "chr7" "chr19" "chr22" "chr17" "chr3"
## [73] "chr8" "chr3" "chr15" "chr6" "chr9" "chr10" "chr6" "chr2" "chr19"
## [82] "chr11" "chr8" "chr17" "chr15" "chr21" "chr7" "chr2" "chr2" "chr3"
```

```
## [91] "chr2" "chr16" "chr10" "chr20" "chr17" "chr13" "chr2" "chr5" "chr14"
## [100] "chr11" "chr8" "chr20" "chr3" "chr7" "chr1" "chr1" "chr3" "chr17"
## [109] "chrX" "chr19" "chr20" "chr6" "chr7" "chr16" "chr7" "chr17" "chr20"
## [118] "chr2" "chr5" "chrX" "chr7" "chr6" "chr19" "chr17" "chr16" "chr5"
## [127] "chr12" "chr9" "chr20" "chr2" "chr12" "chr3" "chr7" "chr2" "chr20"
## [136] "chr20" "chr17" "chr12" "chr19" "chr1" "chr7" "chr20" "chr14" "chr12"
## [145] "chr10" "chr6" "chr9" "chr6" "chr1" "chr18" "chr8" "chr15" "chr6"
## [154] "chr2" "chr1" "chr18" "chr16" "chr9" "chr20" "chr19" "chr17" "chr10"
## [163] "chr6" "chr2" "chrX" "chr16" "chr20" "chr16" "chr20" "chr16" "chr20"
## [172] "chr5" "chr16" "chr17" "chr17" "chr3" "chr8" "chr18" "chr18" "chr7"
## [181] "chr20" "chr16" "chr19" "chr11" "chr12" "chr2" "chr17" "chr1" "chr20"
## [190] "chr4" "chr17" "chr1" "chr6" "chr5" "chr13" "chr7" "chr20" "chr2"
## [199] "chr16" "chr6" "chr11" "chr5" "chr20" "chr1" "chr9" "chr2" "chr16"
## [208] "chr10" "chr9" "chr2" "chr2" "chr21" "chr1" "chr16" "chr18" "chr10"
## [217] "chr16" "chr3" "chr6" "chr16" "chr2" "chr6" "chr10" "chr16" "chr22"
## [226] "chr2" "chr16" "chr8" "chr20" "chr19" "chr16" "chr20" "chr2" "chr3"
## [235] "chr10" "chr14" "chr6" "chr18" "chr15" "chr9" "chr14" "chr7" "chr20"
## [244] "chr3" "chr6" "chr10" "chr4" "chr1" "chr9" "chr15" "chr6" "chr16"
## [253] "chr2" "chr3" "chr14" "chr19" "chr2" "chr5" "chr22" "chr16" "chr6"
## [262] "chr16" "chr17" "chr11" "chr8" "chr3" "chr1" "chr16" "chr21" "chr12"
## [271] "chr16" "chr1" "chr2" "chr2" "chr9" "chr2" "chr16" "chr17" "chr12"
## [280] "chr17" "chr7" "chr20" "chr7" "chr6" "chr12" "chr2" "chr1" "chr5"
## [289] "chr6" "chr2" "chr1" "chr12" "chr2" "chr6" "chr20" "chr2" "chr17"
## [298] "chr3" "chr4" "chr1" "chr17" "chr1" "chr12"
```

```
# make a table of numbers of sequences on each chromosome
table(chr)
```

```
## chr
##          chr1          chr2          chr3
##          18          38          15
##          chr4          chr5          chr6
##           4           8          24
##          chr7          chr8          chr9
##          14          11          12
##          chr10         chr11         chr12
##           9           9          13
##          chr13         chr14         chr15
##           2           8           5
##          chr16         chr17         chr18
##          31          21           6
##          chr19         chr20         chr21
##          16          27           3
##          chr22         chrX          chrY
##           5           4           0
##          chrM chr1_gl000191_random chr1_gl000192_random
##           0           0           0
##          chr4_ctg9_hap1 chr4_gl000193_random chr4_gl000194_random
##           0           0           0
##          chr6_apd_hap1          chr6_cox_hap2          chr6_dbb_hap3
##           0           0           0
##          chr6_mann_hap4          chr6_mcf_hap5          chr6_qbl_hap6
##           0           0           0
##          chr6_ssto_hap7 chr7_gl000195_random chr8_gl000196_random
##           0           0           0
```

```
## chr8_gl000197_random chr9_gl000198_random chr9_gl000199_random
##          0          0          0
## chr9_gl000200_random chr9_gl000201_random chr11_gl000202_random
##          0          0          0
##      chr17_ctg5_hap1 chr17_gl000203_random chr17_gl000204_random
##          0          0          0
## chr17_gl000205_random chr17_gl000206_random chr18_gl000207_random
##          0          0          0
## chr19_gl000208_random chr19_gl000209_random chr21_gl000210_random
##          0          0          0
##      chrUn_gl000211      chrUn_gl000212      chrUn_gl000213
##          0          0          0
##      chrUn_gl000214      chrUn_gl000215      chrUn_gl000216
##          0          0          0
##      chrUn_gl000217      chrUn_gl000218      chrUn_gl000219
##          0          0          0
##      chrUn_gl000220      chrUn_gl000221      chrUn_gl000222
##          0          0          0
##      chrUn_gl000223      chrUn_gl000224      chrUn_gl000225
##          0          0          0
##      chrUn_gl000226      chrUn_gl000227      chrUn_gl000228
##          0          0          0
##      chrUn_gl000229      chrUn_gl000230      chrUn_gl000231
##          0          0          0
##      chrUn_gl000232      chrUn_gl000233      chrUn_gl000234
##          0          0          0
##      chrUn_gl000235      chrUn_gl000236      chrUn_gl000237
##          0          0          0
##      chrUn_gl000238      chrUn_gl000239      chrUn_gl000240
##          0          0          0
##      chrUn_gl000241      chrUn_gl000242      chrUn_gl000243
##          0          0          0
##      chrUn_gl000244      chrUn_gl000245      chrUn_gl000246
##          0          0          0
##      chrUn_gl000247      chrUn_gl000248      chrUn_gl000249
##          0          0          0
```

```
table(chr)[1:24]      # restrict to autosomes, X and Y
```

```
## chr
## chr1 chr2 chr3 chr4 chr5 chr6 chr7 chr8 chr9 chr10 chr11 chr12 chr13
##   18   38   15    4    8   24   14   11   12    9    9   13    2
## chr14 chr15 chr16 chr17 chr18 chr19 chr20 chr21 chr22 chrX  chrY
##    8    5   31   21    6   16   27    3    5    4    0
```

```
# GRanges can be subsetted and ordered
```

```
HepG2[chr=="chr20",]
```

```
## GRanges object with 27 ranges and 7 metadata columns:
```

```
##      seqnames      ranges strand |      name      score      col
##      <Rle>        <IRanges> <Rle> | <numeric> <integer> <logical>
## [1]   chr20      328285-329145   * |      NA          0      <NA>
## [2]   chr20 22410891-22411863   * |      NA          0      <NA>
## [3]   chr20 56039583-56040249   * |      NA          0      <NA>
## [4]   chr20 16455811-16456232   * |      NA          0      <NA>
```

```
## [5] chr20 3140243-3140774 * | NA 0 <NA>
## ... ...
## [23] chr20 5591571-5592037 * | NA 0 <NA>
## [24] chr20 25519664-25520238 * | NA 0 <NA>
## [25] chr20 19900951-19901275 * | NA 0 <NA>
## [26] chr20 35156796-35157140 * | NA 0 <NA>
## [27] chr20 25036720-25037716 * | NA 0 <NA>
## signalValue pValue qValue peak
## <numeric> <numeric> <numeric> <integer>
## [1] 10.808 69.685 5.02806e-66 321
## [2] 6.419 41.020 7.74961e-38 660
## [3] 7.796 36.977 3.66693e-34 315
## [4] 7.351 21.831 1.59668e-19 199
## [5] 7.296 21.587 2.62536e-19 315
## ... ...
## [23] 8.766 11.433 7.67742e-10 249
## [24] 3.300 11.419 7.89520e-10 206
## [25] 4.809 11.155 1.37954e-09 140
## [26] 10.154 10.313 8.30971e-09 163
## [27] 4.381 10.087 1.33278e-08 170
## -----
```

```
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
x = HepG2[order(HepG2),]
seqnames(x) # demonstrate usefulness of Rle type
```

```
## factor-Rle of length 303 with 23 runs
## Lengths: 18 38 15 4 8 ... 16 27 3 5 4
## Values : chr1 chr2 chr3 chr4 chr5 ... chr19 chr20 chr21 chr22 chrX
## Levels(93): chr1 chr2 chr3 ... chrUn_gl000247 chrUn_gl000248 chrUn_gl000249
```

```
as.character(seqnames(x))
```

```
## [1] "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1"
## [10] "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1" "chr1"
## [19] "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2"
## [28] "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2"
## [37] "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2"
## [46] "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2" "chr2"
## [55] "chr2" "chr2" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3"
## [64] "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr3" "chr4"
## [73] "chr4" "chr4" "chr4" "chr5" "chr5" "chr5" "chr5" "chr5" "chr5" "chr5"
## [82] "chr5" "chr5" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6"
## [91] "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6"
## [100] "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr6" "chr7"
## [109] "chr7" "chr7" "chr7" "chr7" "chr7" "chr7" "chr7" "chr7" "chr7" "chr7"
## [118] "chr7" "chr7" "chr7" "chr7" "chr8" "chr8" "chr8" "chr8" "chr8" "chr8"
## [127] "chr8" "chr8" "chr8" "chr8" "chr8" "chr8" "chr9" "chr9" "chr9" "chr9"
## [136] "chr9" "chr9" "chr9" "chr9" "chr9" "chr9" "chr9" "chr9" "chr9" "chr9"
## [145] "chr10" "chr10" "chr10" "chr10" "chr10" "chr10" "chr10" "chr10" "chr10" "chr10"
## [154] "chr11" "chr11" "chr11" "chr11" "chr11" "chr11" "chr11" "chr11" "chr11" "chr11"
## [163] "chr12" "chr12" "chr12" "chr12" "chr12" "chr12" "chr12" "chr12" "chr12" "chr12"
## [172] "chr12" "chr12" "chr12" "chr12" "chr13" "chr13" "chr14" "chr14" "chr14" "chr14"
## [181] "chr14" "chr14" "chr14" "chr14" "chr14" "chr15" "chr15" "chr15" "chr15" "chr15"
## [190] "chr15" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16"
```

```
## [199] "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16"
## [208] "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr16"
## [217] "chr16" "chr16" "chr16" "chr16" "chr16" "chr16" "chr17" "chr17" "chr17" "chr17"
## [226] "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17"
## [235] "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr17" "chr18"
## [244] "chr18" "chr18" "chr18" "chr18" "chr18" "chr18" "chr19" "chr19" "chr19" "chr19"
## [253] "chr19" "chr19" "chr19" "chr19" "chr19" "chr19" "chr19" "chr19" "chr19" "chr19"
## [262] "chr19" "chr19" "chr19" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20"
## [271] "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20"
## [280] "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20" "chr20"
## [289] "chr20" "chr20" "chr20" "chr21" "chr21" "chr21" "chr22" "chr22" "chr22" "chr22"
## [298] "chr22" "chr22" "chrX" "chrX" "chrX" "chrX"
```

## Assessment: Genomic Ranges

```
library(GenomicRanges)
paste("median of signal value column for HepG2 data: ")

## [1] "median of signal value column for HepG2 data: "
median(mcols(HepG2)$signalValue)

## [1] 7.024
paste("chromosome in region with highest signal value: ")

## [1] "chromosome in region with highest signal value: "
max_index <- which.max(mcols(HepG2)$signalValue)
chr = seqnames(HepG2)
as.character(chr)[max_index]

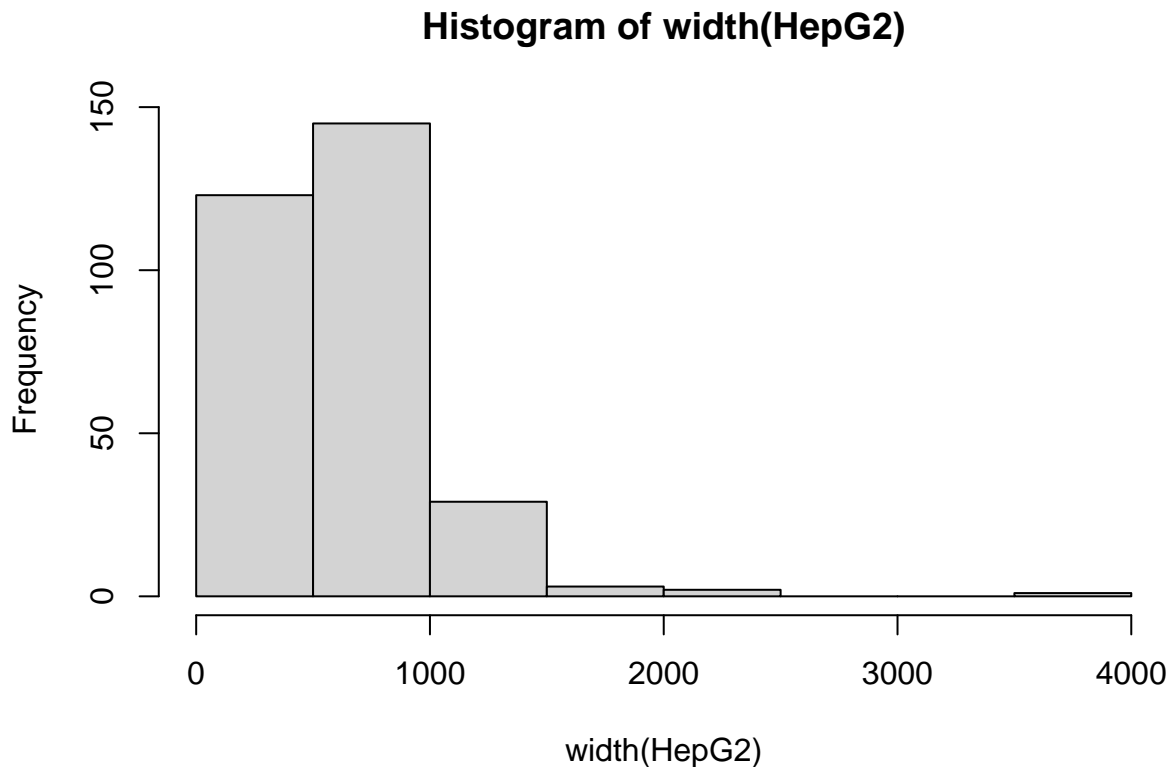
## [1] "chrX"
paste("Number of regions from chromosome 16: ")

## [1] "Number of regions from chromosome 16: "
HepG2[chr == "chr16",]
```

```
## GRanges object with 31 ranges and 7 metadata columns:
##      seqnames      ranges strand |      name      score      col
##      <Rle>        <IRanges> <Rle> | <numeric> <integer> <logical>
## [1] chr16 70191209-70192150   * |      NA          0      <NA>
## [2] chr16 1701039-1702137      * |      NA          0      <NA>
## [3] chr16 25189109-25190026    * |      NA          0      <NA>
## [4] chr16 85325101-85325686    * |      NA          0      <NA>
## [5] chr16 29986461-29986872    * |      NA          0      <NA>
## ...      ...      ...      ... |      ...      ...      ...
## [27] chr16 57481218-57481854      * |      NA          0      <NA>
## [28] chr16 85322504-85322950      * |      NA          0      <NA>
## [29] chr16 19134897-19135280      * |      NA          0      <NA>
## [30] chr16 2586101-2586737        * |      NA          0      <NA>
## [31] chr16 29975932-29976255      * |      NA          0      <NA>
##      signalValue  pValue      qValue      peak
##      <numeric> <numeric> <numeric> <integer>
## [1]      8.371      37.774 8.19277e-35      688
```

```
##      [2]      16.157      36.264 1.65696e-33      783
##      [3]       5.979      31.808 3.44356e-29      606
##      [4]       7.664      31.429 7.88321e-29      223
##      [5]      14.795      29.018 1.73008e-26      198
##      ...      ...      ...      ...
##     [27]       5.126      10.761 3.20978e-09      196
##     [28]       4.331      10.725 3.43494e-09      223
##     [29]       5.380      10.562 4.92563e-09      203
##     [30]       6.521      10.514 5.42123e-09      472
##     [31]       6.897      10.436 6.37196e-09      145
## -----
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
hist(width(HepG2))
```



```
median_width <- median(width(HepG2))
paste("Median width of all chromosomes: ", median_width)
```

```
## [1] "Median width of all chromosomes: 560"
```

## Bioconductor Infrastructure for genomics, microarray and NGS

- IRanges package - representing ranges of integers. Base pair arrangements we want to manipulate in genomics
- Vignette about classes and functions in IRanges package
- Simple functions have good performance
- Summary of most important functions
- IRanges - start, end, width (i.e., 5, 10, 6bP long)



- Start, end, and width functions
- Can specify > 1 range at a time to make IRanges objects of length n
- Intra-range methods:
  - **Shift** - Intra range methods for IRanges - doesn't depend on other ranges contained in IRanges object. I.e., shift IRange to the left by 2.
  - **Narrow** - relative to start, start at nth base pair
  - **Flank** - get flanking sequence 3 base pairs from start or end (start = False). Also bi-directional (both=True)
- Inter-range methods:
  - **range** - will give beginning of the IRanges to the end, including gaps in between
  - **reduce** - gives us base pairs covered by the original ranges (do not get gaps). Can ask for gaps.
  - **disjoint** - set of ranges which has the same coverage as original IRanges object but non-overlapping. Contain union of all endpoints of the original range.

### Assessment: IRanges

```
library(IRanges)
ir <- IRanges(101, 200)
paste("*2 zooms in, giving range with half the width. New starting point: ", start(ir*2))

## [1] "*2 zooms in, giving range with half the width. New starting point: 126"
n_ir <- narrow(ir, start=20)
paste("narrow function with start of 20. New starting point: ", start(n_ir))

## [1] "narrow function with start of 20. New starting point: 120"
paste("+25 operation gives width of resulting range: ", width(ir+25))

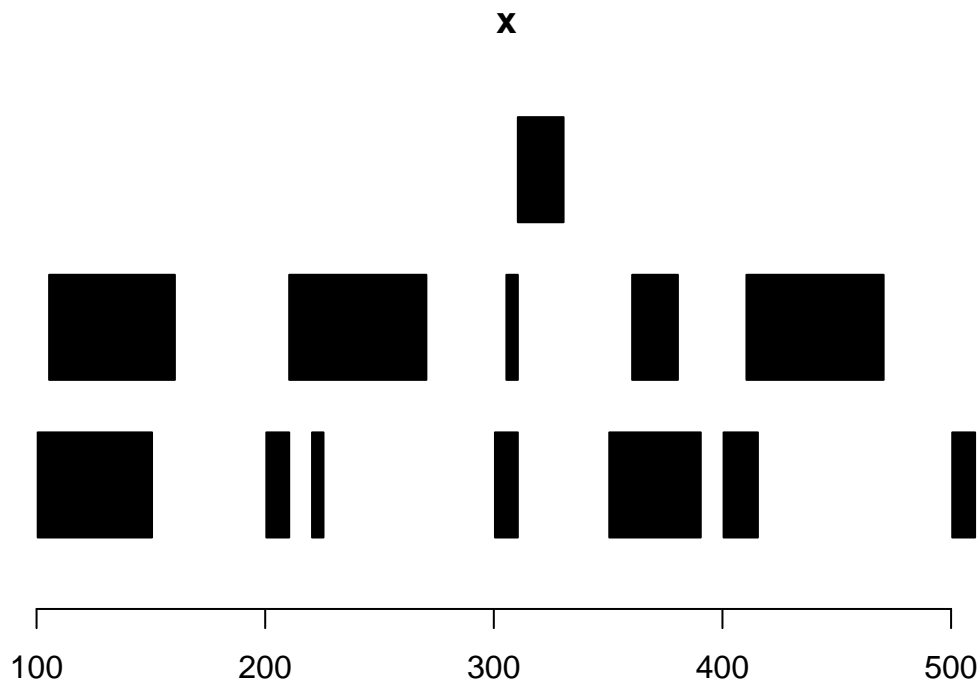
## [1] "+25 operation gives width of resulting range: 150"
m_ir <- IRanges(start=c(1, 11, 21),end=c(3, 15, 27))
paste("sum of widths of multiple IRanges objects:", sum(width(m_ir)))

## [1] "sum of widths of multiple IRanges objects: 15"
x <- IRanges(start=c(101,106,201,211,221,301,306,311,351,361,401,411,501), end=c(150,160,210,270,225,310,320,350,360,400,410,500),
library(ph525x)

## Loading required package: png
## Loading required package: grid
## Loading required package: Biobase
## Welcome to Bioconductor
##
## Vignettes contain introductory material; view with
## 'browseVignettes()'. To cite Bioconductor, see
## 'citation("Biobase")', and for packages 'citation("pkgname)".

## Loading required package: Homo.sapiens
## Loading required package: AnnotationDbi
```

```
## Loading required package: OrganismDbi
## Loading required package: GenomicFeatures
## Warning: package 'GenomicFeatures' was built under R version 4.0.4
## Loading required package: GO.db
##
## Loading required package: org.Hs.eg.db
##
## Loading required package: TxDb.Hsapiens.UCSC.hg19.knownGene
plotRanges(x)
```



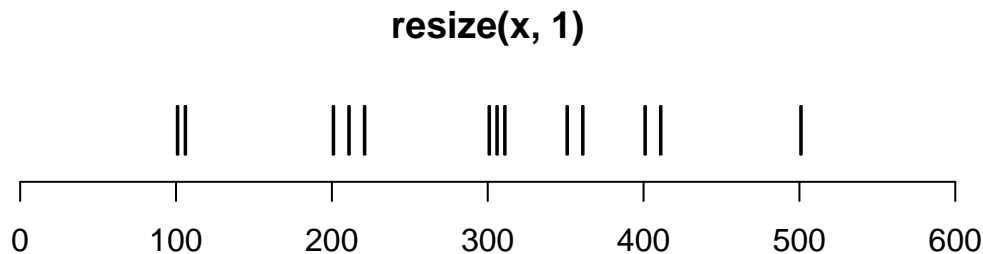
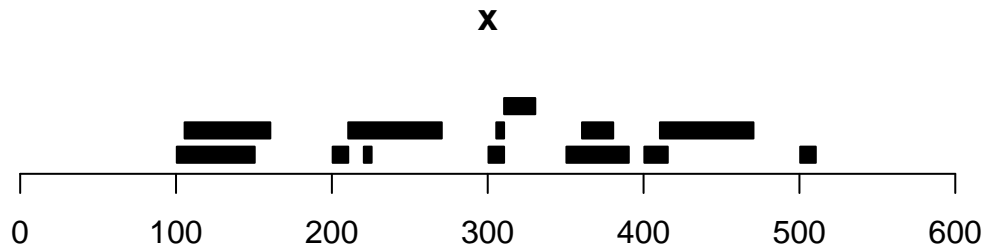
```
paste("Total width not covered by ranges in x:", sum(width(gaps(x))))
```

```
## [1] "Total width not covered by ranges in x: 130"
```

```
paste("Number of disjoint ranges within ranges in x:", length(disjoin(x)))
```

```
## [1] "Number of disjoint ranges within ranges in x: 17"
```

```
par(mfrow=c(2, 1))
plotRanges(x, xlim=c(0, 600))
plotRanges(resize(x, 1), xlim=c(0, 600))
```



## Genomic ranges: GRanges

- Extension of IRanges
- Contain a sequence name - IRanges of chromosome Z.
- Can contain chromosome information and sequence length
- Sequence names as Rle
- IRanges and strand as Rle also
- Can shift similar to IRanges - will go off end of chromosome if exceeds length
- Wrap in trim function to make sure that the end at chromosome end does not exceed
- Metadata accessed with *mcols*
- Can add cols by *mcols\$*
- Additional package called *GRangesList* - groups GRanges together by wrapping in function call
- Example of *GRangesList* - grouping exons by gene or by transcript
- Application of package - find overlaps between GRanges objects
- *findOverlaps* function - query and subject (see in *help()* function)
- output of *findOverlaps* is a hits object with length representing # overlaps
- Same way to get the overlaps is *%over%* function - which returns logical vector
- *Rle* object defined by IRanges but similar object in base R = Run length encoding
- If vector repeats certain values, can save memory by number and number of times repeated
- *str* function gives us the compact representation
- Peering into *Rle* object - can use *Views* object to see *IRanges* from start to end. Only a virtual class - saves *Rle* and number of views / windows into it
- Can also use for *Fasta* files or other objects

## Assessment: GRanges

- GRanges object extends concept of interval ranges
- Ranges can be defined by:
  - chromosome we are referring to (seqnames in Bioconductor)
  - strand of DNA we are referring to (+ or -)

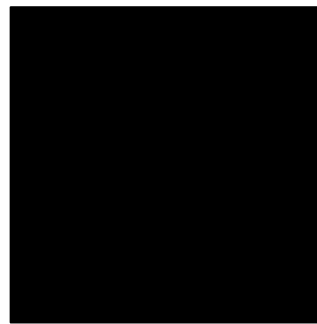
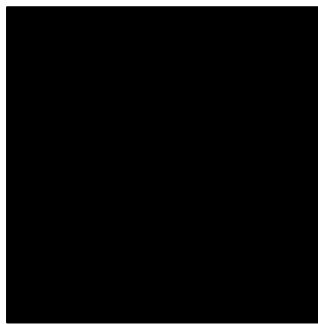
- These two pieces of information are necessary for specification of a range of DNA

```
library(GenomicRanges)
library(IRanges)
library(ph525x)
x = GRanges("chr1", IRanges(c(1,101),c(50,150)), strand=c("+","-"))
paste("Get the internal IRanges from a GRanges object: ")
```

```
## [1] "Get the internal IRanges from a GRanges object: "
```

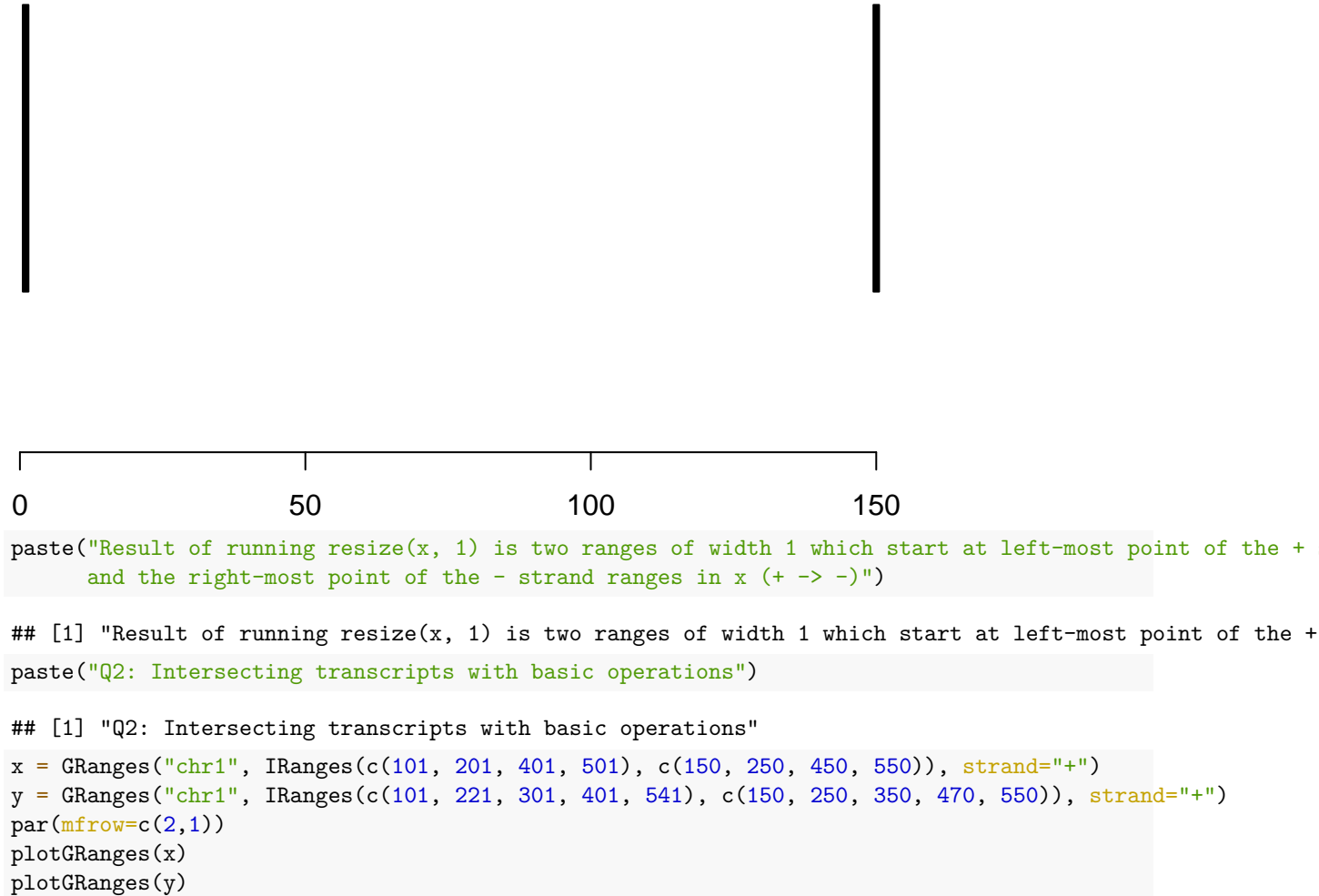
```
plotGRanges = function(x) plotRanges(ranges(x))
plotGRanges(x)
```

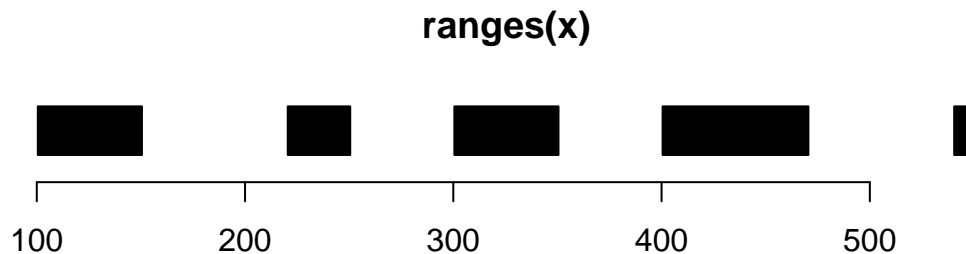
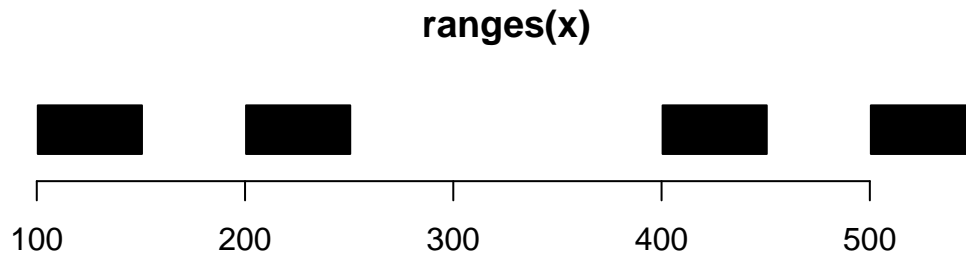
**ranges(x)**



```
plotGRanges(resize(x, 1))
```

## ranges(x)





```
multiple_granges_list <- GRangesList(x,y)
single_granges_list <- GRangesList(c(x, y))

findOverlaps(x, y)

## Hits object with 4 hits and 0 metadata columns:
##      queryHits subjectHits
##      <integer>  <integer>
## [1]          1          1
## [2]          2          2
## [3]          3          4
## [4]          4          5
## -----
## queryLength: 4 / subjectLength: 5

paste("width of overlap between x and y: ", sum(width(union(x, y))) - sum(width(intersect(x, y))))

## [1] "width of overlap between x and y:  130"

z = GRanges("chr1", range(ranges(x)), strand="-")
```

## Operating on GRanges

- Small set of ranges = intervals on chromosome
- Operations:
  - *reduce* - project all of the occupied bases into contiguous intervals and leaves empty parts with no coverage
  - *disjoin* - set of intervals / ranges generated by disjoin of set of ranges. Same occupancy as original GRanges object
    - \* Maximal complexity set of intervals where wherever there was an endpoint, we will not cross in a set of ranges.

- *gap* - set xlim to show the regions that are never expressed. could be regarded as introns, spliced out. (gaps of exons are introns)
- Elaborate the set of intervals by turning it into a GRanges object by specifying seqnames and range information.
- Metadata that should be specified - strand information, genome, seqlengths, seqinfo
- How to pick out transcription start sites - plot overlapping genes. Resize with argument 1 to get down to one base from start. Gives us the addresses of start sites
- Finding promoters - interval of three bases upstream of bases upstream is regarded as a promoter. Use *flank* operation with argument 3 - gives us the locations of the upstream promoters. Use start=FALSE to indicate flank at the end of the interval rather than start.

## Finding Overlaps

- Example: finding genes that are close to reported binding sites and add some annotation to those genes
- HepG2 + GM12878 - reported binding sites for 2 cell lines
- Want to find the genes that are nearest to them. Instead of separately, create a consensus GRanges which includes only sites that are common to both GRanges
- Function: *findOverlaps* uses query and subject - for each range, see if it appears in another range and return pair. Returns object of class *hits*. Only want the ones where there is a hit - use *queryHits* function and subset based on queryHits
- Extract just region information using *granges* function
- Show extraction of genes in next video, and matching of the regions in ERBS dataset to genes

```
# load packages
library(GenomicFeatures)
library(GenomicRanges)
library(IRanges)
library(ERBS)

# load ESRRR ChIP data
data(HepG2)
data(GM12878)

# browseVignettes("GenomicRanges")

# find binding sites common to both HepG2 and GM12878
?findOverlaps

## Help on topic 'findOverlaps' was found in the following packages:
##
##   Package      Library
##   SummarizedExperiment /Library/Frameworks/R.framework/Versions/4.0/Resources/library
##   GenomicRanges      /Library/Frameworks/R.framework/Versions/4.0/Resources/library
##   GenomicAlignments  /Library/Frameworks/R.framework/Versions/4.0/Resources/library
##   IRanges            /Library/Frameworks/R.framework/Versions/4.0/Resources/library
##
##
## Using the first match ...
# for each row in query, return overlapping row in subject
res = findOverlaps(HepG2, GM12878)
class(res)

## [1] "SortedByQueryHits"
```

```
## attr("package")
## [1] "S4Vectors"
res

## Hits object with 75 hits and 0 metadata columns:
##      queryHits subjectHits
##      <integer>  <integer>
##      [1]         1         12
##      [2]         2         78
##      [3]         4        777
##      [4]         5          8
##      [5]         8         13
##      ...         ...         ...
##     [71]        285        621
##     [72]        287        174
##     [73]        291       1855
##     [74]        294        512
##     [75]        300        144
## -----
##  queryLength: 303 / subjectLength: 1873
# ranges from the query for which we found a hit in the subject
index = queryHits(res)
erbs = HepG2[index,]
erbs

## GRanges object with 75 ranges and 7 metadata columns:
##      seqnames      ranges strand |      name      score      col
##      <Rle>        <IRanges> <Rle> | <numeric> <integer> <logical>
##      [1]    chr2    20335378-20335787 * |      NA          0      <NA>
##      [2]   chr20    328285-329145    * |      NA          0      <NA>
##      [3]   chr19   1244419-1245304    * |      NA          0      <NA>
##      [4]   chr11   64071828-64073069 * |      NA          0      <NA>
##      [5]    chr2   16938364-16938840 * |      NA          0      <NA>
##      ...         ...         ...   ... |      ...         ...      ...
##     [71]   chr12 118558730-118559158 * |      NA          0      <NA>
##     [72]    chr1   35331750-35332300 * |      NA          0      <NA>
##     [73]    chr1   26146200-26147004 * |      NA          0      <NA>
##     [74]    chr6   44224657-44225693 * |      NA          0      <NA>
##     [75]    chr1 110198573-110199126 * |      NA          0      <NA>
##      signalValue  pValue    qValue    peak
##      <numeric> <numeric> <numeric> <integer>
##      [1]      58.251    75.899 6.14371e-72      195
##      [2]      10.808    69.685 5.02806e-66      321
##      [3]      12.427    43.855 1.35976e-40      604
##      [4]      10.850    40.977 7.33386e-38      492
##      [5]      12.783    38.004 5.36029e-35      255
##      ...         ...         ...         ...
##     [71]       8.292    10.294 8.59089e-09      195
##     [72]      10.458    10.233 9.81822e-09      341
##     [73]       5.742    10.176 1.10429e-08      337
##     [74]       3.525    10.102 1.29621e-08      838
##     [75]       7.929    10.047 1.44208e-08      197
## -----
##  seqinfo: 93 sequences (1 circular) from hg19 genome
```



```
# extract only the ranges
granges(erbs)
```

```
## GRanges object with 75 ranges and 0 metadata columns:
```

```
##      seqnames      ranges strand
##      <Rle>        <IRanges> <Rle>
## [1]   chr2    20335378-20335787      *
## [2]  chr20     328285-329145      *
## [3]  chr19    1244419-1245304      *
## [4]  chr11    64071828-64073069     *
## [5]   chr2    16938364-16938840     *
## ...      ...                ...
## [71] chr12 118558730-118559158      *
## [72] chr1   35331750-35332300      *
## [73] chr1   26146200-26147004      *
## [74] chr6   44224657-44225693      *
## [75] chr1  110198573-110199126      *
## -----
```

```
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
erbs
```

```
## GRanges object with 75 ranges and 7 metadata columns:
```

```
##      seqnames      ranges strand |      name      score      col
##      <Rle>        <IRanges> <Rle> | <numeric> <integer> <logical>
## [1]   chr2    20335378-20335787      * |      NA          0      <NA>
## [2]  chr20     328285-329145      * |      NA          0      <NA>
## [3]  chr19    1244419-1245304      * |      NA          0      <NA>
## [4]  chr11    64071828-64073069     * |      NA          0      <NA>
## [5]   chr2    16938364-16938840     * |      NA          0      <NA>
## ...      ...                ...   |      ...        ...      ...
## [71] chr12 118558730-118559158      * |      NA          0      <NA>
## [72] chr1   35331750-35332300      * |      NA          0      <NA>
## [73] chr1   26146200-26147004      * |      NA          0      <NA>
## [74] chr6   44224657-44225693      * |      NA          0      <NA>
## [75] chr1  110198573-110199126      * |      NA          0      <NA>
```

```
##      signalValue    pValue      qValue      peak
##      <numeric> <numeric> <numeric> <integer>
## [1]      58.251      75.899 6.14371e-72      195
## [2]      10.808      69.685 5.02806e-66      321
## [3]      12.427      43.855 1.35976e-40      604
## [4]      10.850      40.977 7.33386e-38      492
## [5]      12.783      38.004 5.36029e-35      255
## ...      ...                ...   ...
## [71]       8.292      10.294 8.59089e-09      195
## [72]      10.458      10.233 9.81822e-09      341
## [73]       5.742      10.176 1.10429e-08      337
## [74]       3.525      10.102 1.29621e-08      838
## [75]       7.929      10.047 1.44208e-08      197
```

```
## -----
```

```
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

## Assessment: Finding Overlaps

```
library(ERBS)
data(HepG2)
data(GM12878)
paste("17th region of HepG2 starts at:", start(granges(HepG2[17])))

## [1] "17th region of HepG2 starts at: 46528596"

dtn <- distanceToNearest(HepG2[17], GM12878)
gm_idx <- subjectHits(dtn)
start_site <- start(GM12878[gm_idx])
distance_to_closest = mcols(dtn)$distance
paste("Start site of closest region to 17th region of HepG2: ", start_site)

## [1] "Start site of closest region to 17th region of HepG2: 46524762"
paste("Distance between closest region to 17th region of HepG2: ", distance_to_closest)

## [1] "Distance between closest region to 17th region of HepG2: 2284"
X <- vector(mode="integer", length=length(HepG2))
for(i in seq_along(HepG2)) {
  closest_region = distanceToNearest(HepG2[i], GM12878)
  distance = mcols(closest_region)$distance
  X[i] = distance
}
proportion_lt_2k_bp <- length(X[X < 2000]) / length(X)
paste("proportion of distances < 2000 bp: ", proportion_lt_2k_bp)

## [1] "proportion of distances < 2000 bp: 0.267326732673267"
```

## Genes as GRanges

- Mapping genes to binding sites
- Load Gene information from homo sapiens library and extract genes using function called **genes** - returns GRanges

```
library(Homo.sapiens)
library(ERBS)
ghs = genes(Homo.sapiens)

## 403 genes were dropped because they have exons located on both strands
## of the same reference sequence or on more than one reference sequence,
## so cannot be represented by a single genomic range.
## Use 'single.strand.genes.only=FALSE' to get all the genes in a
## GRangesList object, or use suppressMessages() to suppress this message.

res = precede(erbs, ghs)
res

## [1] 22817 16173 21772 7870 20199 22131 13257 20469 21943 8564 19061 15836
## [13] 21282 8959 278 14620 1657 22774 21746 10777 14568 20910 6626 12830
## [25] 9838 19991 21643 15740 12911 13326 8303 20834 934 10485 23027 4443
## [37] 6613 21335 21125 14508 15979 2693 4122 9485 17665 18376 17932 2696
## [49] 16990 16952 15735 9386 1642 3634 6037 20891 15062 1779 3316 11746
## [61] 12168 21689 22406 19979 14099 13558 3653 6077 21280 9705 13095 3322
```

```
## [73] 6343 1553 9552
```

```
ghs[res[1:3]]
```

```
## GRanges object with 3 ranges and 1 metadata column:
```

```
##      seqnames      ranges strand |      GENEID
##      <Rle>        <IRanges> <Rle> | <CharacterList>
##    9741      chr2 20232411-20251789 - |      9741
##   57761     chr20   361308-378203  + |      57761
##   90007     chr19  1248552-1259142  + |      90007
## -----
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

- Start and end of genes - series of locations. Also have ID used by Homo sapiens database to match gene info across different databases
- Gene with ID 1 is in chromosome 19. Start defined in IRanges.
- **strand** tells you which of two DNA strands the gene is on. When gene expression happens, DNA opens up and code for gene could be in either strand.
- Movement of the transcription is going in a certain direction
- Large -> small if -, small -> large if +.
- Transcription start site - depends on strand information
- Function from **GenomicRanges** package called **precede** - tells you what is ahead of the transcription start site which varies depending on strand
- Finds entry and query closest to subject only when in front of.
- Moving towards report on which genes are closest to binding sites

## Assessment: Genes as GRanges

```
library(Homo.sapiens)
ghs = genes(Homo.sapiens)
```

```
## 403 genes were dropped because they have exons located on both strands
## of the same reference sequence or on more than one reference sequence,
## so cannot be represented by a single genomic range.
## Use 'single.strand.genes.only=FALSE' to get all the genes in a
## GRangesList object, or use suppressMessages() to suppress this message.
```

```
number_of_genes <- length(ghs)
```

```
paste("number of genes represented: ", number_of_genes)
```

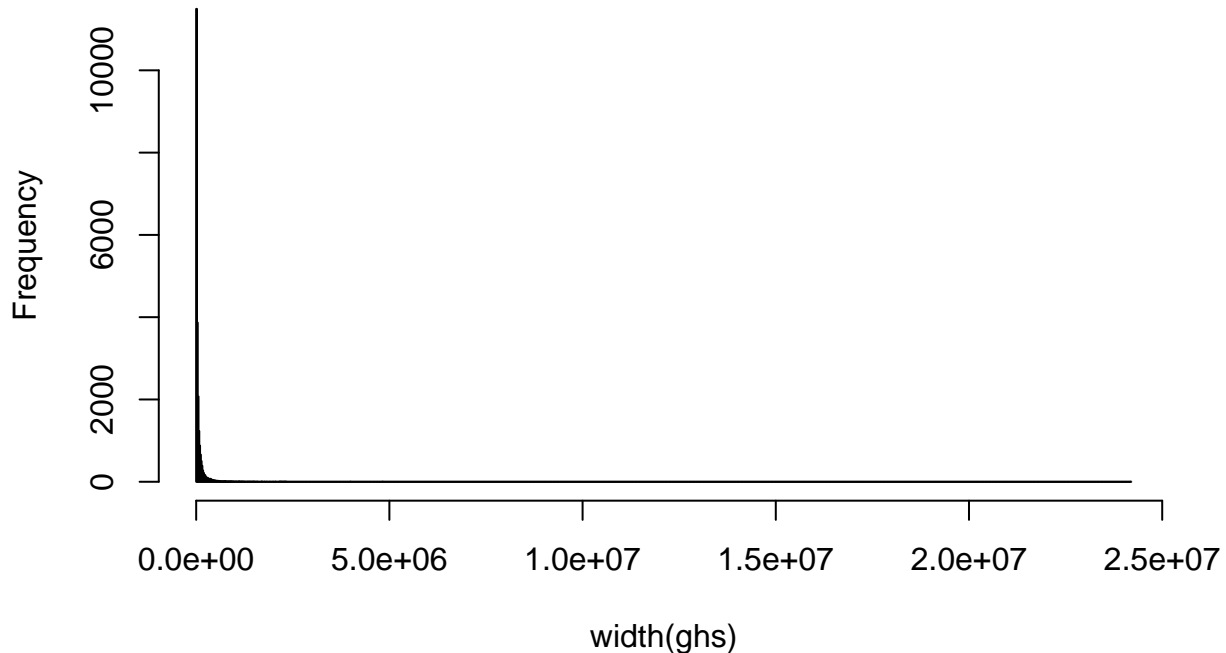
```
## [1] "number of genes represented: 23056"
```

```
chr_most_genes <- names(which.max(table(as.vector(seqnames(ghs)))))
paste("chromosome with most genes: ", chr_most_genes)
```

```
## [1] "chromosome with most genes: chr1"
```

```
hist(width(ghs), nc=1000)
```

## Histogram of width(ghs)



```
median_width <- median(width(ghs))  
  
paste("median gene width: ", median_width)
```

```
## [1] "median gene width: 20115.5"
```

## Finding the Nearest Gene

- Compute distance between each binding site and corresponding gene found with precede, use **distance** function
- Takes two GRanges objects, and the genes we have found with precede
- We expect overlaps, however will not show up because we are requiring binding sites precede the genes

```
library(Homo.sapiens)  
ghs = genes(Homo.sapiens)
```

```
## 403 genes were dropped because they have exons located on both strands  
## of the same reference sequence or on more than one reference sequence,  
## so cannot be represented by a single genomic range.  
## Use 'single.strand.genes.only=FALSE' to get all the genes in a  
## GRangesList object, or use suppressMessages() to suppress this message.
```

```
library(ERBS)  
index = precede(erbs, ghs)  
ghs[index[1:3]]
```

```
## GRanges object with 3 ranges and 1 metadata column:  
##      seqnames      ranges strand |      GENEID
```

```
##          <Rle>          <IRanges> <Rle> | <CharacterList>
##    9741      chr2 20232411-20251789      - |          9741
##   57761    chr20    361308-378203      + |          57761
##   90007    chr19   1248552-1259142      + |          90007
## -----
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
erbs[1:3]
```

```
## GRanges object with 3 ranges and 7 metadata columns:
##      seqnames      ranges strand |      name      score      col
##      <Rle>      <IRanges> <Rle> | <numeric> <integer> <logical>
## [1]      chr2 20335378-20335787      * |          NA          0      <NA>
## [2]     chr20   328285-329145      * |          NA          0      <NA>
## [3]     chr19 1244419-1245304      * |          NA          0      <NA>
##      signalValue    pValue      qValue      peak
##      <numeric> <numeric>    <numeric> <integer>
## [1]      58.251     75.899 6.14371e-72      195
## [2]      10.808     69.685 5.02806e-66      321
## [3]      12.427     43.855 1.35976e-40      604
## -----
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
distance(erbs, ghs[index])
```

```
## [1] 83588 32162 3247 12490 91229 125579 95887 203084 26140
## [10] 4342 1158347 30950 82008 20658 32087 19444 74549 5110
## [19] 14252 48739 11043 29669 24061 22090 1989458 77873 343959
## [28] 30283 14601 48298 23414 5533 23832 962904 4678 12616
## [37] 13959 141321 75543 19992 25200 29955 26967 22447 82062
## [46] 12918 880 67725 177905 72543 26399 41808 676 437226
## [55] 270972 105665 60815 82132 40245 14666 74833 127391 10252
## [64] 140320 14696 39814 5507 444 195514 72907 14711 6332
## [73] 201266 2634 31291
```

```
tssgr = resize(ghs, 1) # shrink down to one going in direction towards transcription start site, aware
tssgr
```

```
## GRanges object with 23056 ranges and 1 metadata column:
```

```
##      seqnames      ranges strand |      GENEID
##      <Rle> <IRanges> <Rle> | <CharacterList>
##      1      chr19 58874214      - |          1
##     10      chr8 18248755      + |          10
##    100     chr20 43280376      - |          100
##   1000     chr18 25757445      - |          1000
##  10000     chr1 244006886      - |         10000
##      ...      ...      ...      ...      ...
##   9991     chr9 115095944      - |          9991
##   9992    chr21 35736323      + |          9992
##   9993    chr22 19109967      - |          9993
##   9994     chr6 90539619      + |          9994
##   9997    chr22 50964905      - |          9997
## -----
```

```
## seqinfo: 93 sequences (1 circular) from hg19 genome
```

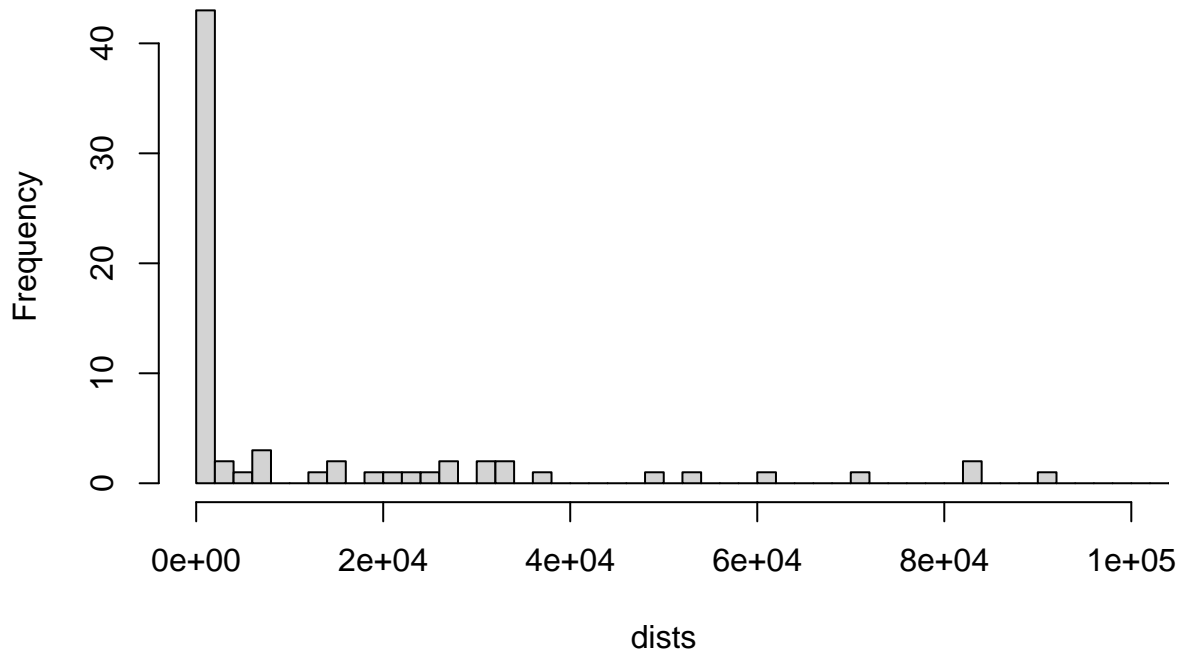
```
d=distanceToNearest(erbs, tssgr)
```

```
queryHits(d)
```

```
## [1] 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
## [26] 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50
## [51] 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75
```

```
dists = values(d)$distance
hist(dists,nc=1000,xlim=c(0,100000))
```

## Histogram of dists



```
index = subjectHits(d)[dists < 1000]
index
```

```
## [1] 19883 6316 18488 14325 9348 19622 19678 16536 4171 13017 21240 22438
## [13] 10812 20840 13796 8334 2185 2917 16265 6286 21787 14490 17932 13607
## [25] 3681 1642 21117 2204 14339 12775 13722 16883 19605 15633 7235 6077
## [37] 14605 3119 15380 10503 9555
```

- define another distance: ask for each binding site, find the transcription start site that is closest
- For each of our binding sites, find the closest transcription start site using **distanceToNearest**. Finds distance to nearest given query and subject
- Now, we have zeros because there is overlap. Output is a **hits** object. Need to use **queryHits** rather than subsetting.
- For distance, use **values** function to extract columns and grab distance
- Index of genes that are closest using **subjectHits**
- Find genes that are closer than 1k to binding sites
- Use genes that were found to be close, and get further information

## Annotating Genes

- Use `select` function to query Homo sapiens database
- Need to give: key, columns we want to look at, key type
- Example of going from ranges to list of interesting genes

```
library(Homo.sapiens)
library(ERBS)
ghs = genes(Homo.sapiens)
```

```
## 403 genes were dropped because they have exons located on both strands
## of the same reference sequence or on more than one reference sequence,
## so cannot be represented by a single genomic range.
## Use 'single.strand.genes.only=FALSE' to get all the genes in a
## GRangesList object, or use suppressMessages() to suppress this message.
```

```
tssgr = resize(ghs, 1) # shrink down to one going in direction towards transcription start site, aware
d=distanceToNearest(erbs, tssgr)
dists = values(d)$distance
index = subjectHits(d)[dists < 1000]
tssgr[index,]
```

```
## GRanges object with 41 ranges and 1 metadata column:
##      seqnames      ranges strand |      GENEID
##      <Rle> <IRanges> <Rle> | <CharacterList>
##      80023      chr20      327370      + |      80023
##      2101       chr11     64073044      + |      2101
##      7086       chr3      53290130      - |      7086
##      5478       chr7      44836241      + |      5478
##      286262      chr9     140095163      - |      286262
##      ...      ...      ...      ... .      ...
##      55090      chr17     17380300      + |      55090
##      11165      chr6      34360457      - |      11165
##      56181      chr1      26146397      + |      56181
##      347734      chr6      44225283      - |      347734
##      2948       chr1     110198698      + |      2948
##      -----
##      seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
keytypes(Homo.sapiens)
```

```
## [1] "ACCNUM"      "ALIAS"      "CDSID"      "CDSNAME"    "DEFINITION"
## [6] "ENSEMBL"     "ENSEMBLPROT" "ENSEMBLTRANS" "ENTREZID"   "ENZYME"
## [11] "EVIDENCE"    "EVIDENCEALL" "EXONID"     "EXONNAME"   "GENEID"
## [16] "GENENAME"    "GO"         "GOALL"      "GOID"       "IPI"
## [21] "MAP"         "OMIM"       "ONTOLOGY"   "ONTOLOGYALL" "PATH"
## [26] "PFAM"        "PMID"       "PROSITE"    "REFSEQ"     "SYMBOL"
## [31] "TERM"        "TXID"       "TXNAME"     "UCSCKG"     "UNIGENE"
## [36] "UNIPROT"
```

```
keys = as.character(values(tssgr[index])$GENEID)
columns(Homo.sapiens)
```

```
## [1] "ACCNUM"      "ALIAS"      "CDSCHROM"   "CDSSEND"    "CDSID"
## [6] "CDSNAME"     "CDSSTART"   "CDSSTRAND"  "DEFINITION" "ENSEMBL"
## [11] "ENSEMBLPROT" "ENSEMBLTRANS" "ENTREZID"   "ENZYME"     "EVIDENCE"
## [16] "EVIDENCEALL" "EXONCHROM"  "EXONEND"    "EXONID"     "EXONNAME"
```

```
## [21] "EXONRANK"      "EXONSTART"      "EXONSTRAND"      "GENEID"          "GENENAME"
## [26] "GO"            "GOALL"           "GOID"            "IPI"             "MAP"
## [31] "OMIM"          "ONTOLOGY"        "ONTOLOGYALL"     "PATH"            "PFAM"
## [36] "PMID"          "PROSITE"         "REFSEQ"          "SYMBOL"          "TERM"
## [41] "TXCHROM"       "TXEND"           "TXID"            "TXNAME"          "TXSTART"
## [46] "TXSTRAND"      "TXTYPE"          "UCSCCKG"         "UNIGENE"         "UNIPROT"
```

```
res = select(Homo.sapiens, keys = keys,
              columns = c("SYMBOL", "GENENAME"), keytype="GENEID")
```

```
## 'select()' returned 1:1 mapping between keys and columns
```

```
res[1:2,]
```

```
##      GENEID                GENENAME SYMBOL
## 1   80023                neurensin 2  NRSN2
## 2   2101 estrogen related receptor alpha  ESRRA
```

## Assessment: Finding and getting annotation for closest gene

- Find the closest genes to some of our binding sites - use consensus set of regions

```
library(ERBS)
data(HepG2)
data(GM12878)
res = findOverlaps(HepG2,GM12878)
erbs = HepG2[queryHits(res)]
erbs = granges(erbs)

erbs2= intersect(HepG2,GM12878)

erbs
```

```
## GRanges object with 75 ranges and 0 metadata columns:
##      seqnames      ranges strand
##      <Rle>         <IRanges> <Rle>
##      [1]      chr2  20335378-20335787      *
##      [2]      chr20 328285-329145      *
##      [3]      chr19 1244419-1245304      *
##      [4]      chr11 64071828-64073069      *
##      [5]      chr2 16938364-16938840      *
##      ...      ...      ...      ...
##      [71]     chr12 118558730-118559158      *
##      [72]      chr1 35331750-35332300      *
##      [73]      chr1 26146200-26147004      *
##      [74]      chr6 44224657-44225693      *
##      [75]      chr1 110198573-110199126      *
##      -----
##      seqinfo: 93 sequences (1 circular) from hg19 genome
```

```
erbs2
```

```
## GRanges object with 75 ranges and 0 metadata columns:
##      seqnames      ranges strand
##      <Rle>         <IRanges> <Rle>
##      [1]      chr1 16339152-16339862      *
##      [2]      chr1 26146200-26147004      *
```



```
##      [3]      chr1      32879507-32879907      *
##      [4]      chr1      35331750-35332300      *
##      [5]      chr1     102900017-102900356      *
##      ...      ...      ...      ...
##      [71]     chr20      62586998-62587997      *
##      [72]     chr22      29977062-29977454      *
##      [73]      chrX       1510388-1511745      *
##      [74]      chrX       26801642-26802021      *
##      [75]      chrX       54466501-54466956      *
##      -----
##      seqinfo: 93 sequences (1 circular) from hg19 genome

library(Homo.sapiens)
ghs = genes(Homo.sapiens)

##      403 genes were dropped because they have exons located on both strands
##      of the same reference sequence or on more than one reference sequence,
##      so cannot be represented by a single genomic range.
##      Use 'single.strand.genes.only=FALSE' to get all the genes in a
##      GRangesList object, or use suppressMessages() to suppress this message.

transcription_start_site=resize(ghs["100113402"], 1)
paste("transcription start site for gene id 100113402: ", transcription_start_site)

## [1] "transcription start site for gene id 100113402:  chr16:70563402:+"

library(ERBS)
data(HepG2)
data(GM12878)
res = findOverlaps(HepG2,GM12878)
erbs = HepG2[queryHits(res)]
erbs = granges(erbs)
index = nearest(erbs[4], tssgr)
index

## [1] 6316

gene_id <- names(tssgr[index,]$GENEID)

paste("gene id with TSS closest to 4th region of erbs: ", gene_id)

## [1] "gene id with TSS closest to 4th region of erbs:  2101"

keys = as.character(values(tssgr[index])$GENEID)
symbol_of_gene <- select(Homo.sapiens, keys=keys, columns=c("SYMBOL"), keytype="GENEID")

## 'select()' returned 1:1 mapping between keys and columns

paste("Symbol of gene id: ", symbol_of_gene$SYMBOL)

## [1] "Symbol of gene id:  ESRRA"
```