IRanges

Bioconductor Infrastructure for Sequence Analysis

November 24, 2009

Outline

IRanges

- Supports the manipulation and analysis of:
  - Sequences (ordered collections of elements)
  - Ranges of indices into sequences
  - Data on ranges
- Emphasis on efficiency in space and time
- Metadata scheme for self-documenting objects and reproducible analysis

IRanges and High-throughput Sequencing

- The basis of much of the sequence analysis functionality in Bioconductor
- Representation of information on chromosomes/contigs
  - Intervals with or without associated data
  - Piecewise constant measures (e.g. coverage)
- Vector and interval operations for these representations
  - Interval overlap calculations
  - Coverage within peak regions

The Two Towers of IRanges

- *RleList* - coverage (or other piecewise constant measures) on chromosomes/contigs. RLE is an initialism for run length encoding, a standard compression method in signal processing.
- *RangedData* - intervals and associated data on chromosomes/contigs. Essentially a data table that is sorted by the chromosomes/contigs indicator column.

Outline

The Foundation of IRanges

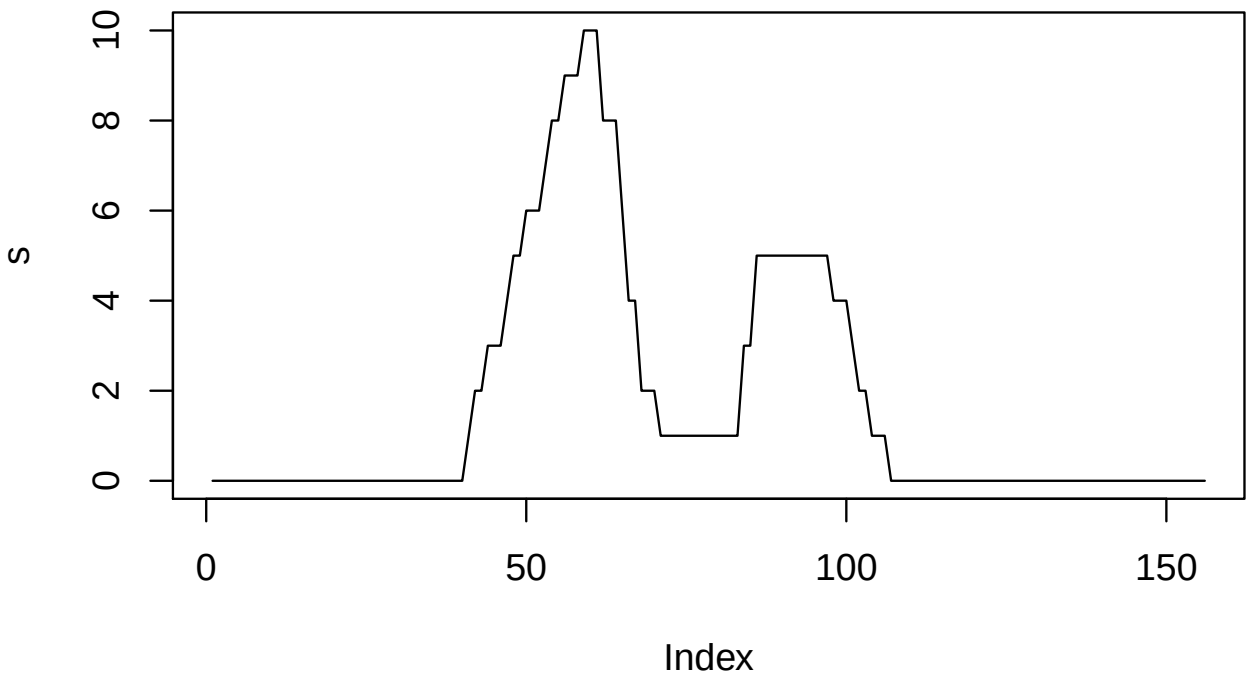
Almost every object manipulated by *IRanges* is a sequence:

- Atomic sequences (e.g. R vectors)
- Lists
- Data tables (two dimensions)

Positional Piecewise Constant Measures

- The number of genomic positions in a genome is often in the billons for higher organisms, making it challenging to represent in memory.
- Some data across a genome tend to be sparse (i.e. large stretches of "no information")
- The *IRanges* packages solves the set of problems for positional measures that tend to have consecutively repeating values.
- The *IRanges* package *does not* address the problem of positional measures that constantly fluxuate, such as conservation scores.

Example sequence



Run-Length Encoding (RLE)

Our example has many repeated values:

Code

```
> sum(diff(s) == 0)

[1] 133
```

Good candidate for compression by run-length encoding:

Code

```
> sRle <- Rle(s)
> sRle

'numeric' Rle of length 156 with 23 runs
  Lengths:  40 1 2 3 1 2 3 1 2 3 ...
  Values :  0 1 2 3 4 5 6 7 8 9 ...
```

Compression reduces size from 156 to 46.

Rle operations

The *Rle* object like any other sequence/vector:

Basic

```
> sRle > 0 | rev(sRle) > 0
```

```
'logical' Rle of length 156 with 3 runs
  Lengths:  40 76 40
  Values :  FALSE TRUE FALSE
```

Summary

```
> sum(sRle > 0)
```

```
[1] 66
```

Statistics

```
> cor(sRle, rev(sRle))
```

```
[1] 0.5142557
```

Splitting up *Rle* by sequence

Code

```
> print(sRleList <- split(sRle, rep(c("chr1",
+     "chr2"), each = length(sRle)/2)))

CompressedRleList of length 2
$chr1
'numeric' Rle of length 78 with 16 runs
  Lengths:  40 1 2 3 1 2 3 1 2 3 ...
  Values :  0 1 2 3 4 5 6 7 8 9 ...

$chr2
'numeric' Rle of length 78 with 8 runs
  Lengths:  5 2 12 3 1 2 3 50
  Values :  1 3 5 4 3 2 1 0
```

RleList supports most *Rle* operations, element-wise.

EXternal sequences

- Sequences derived from *XSequence* are references
- Memory not copied when containing object is modified
- Example: *XString* in *Biostrings* package, for storing biological sequences efficiently

Outline

Ranges

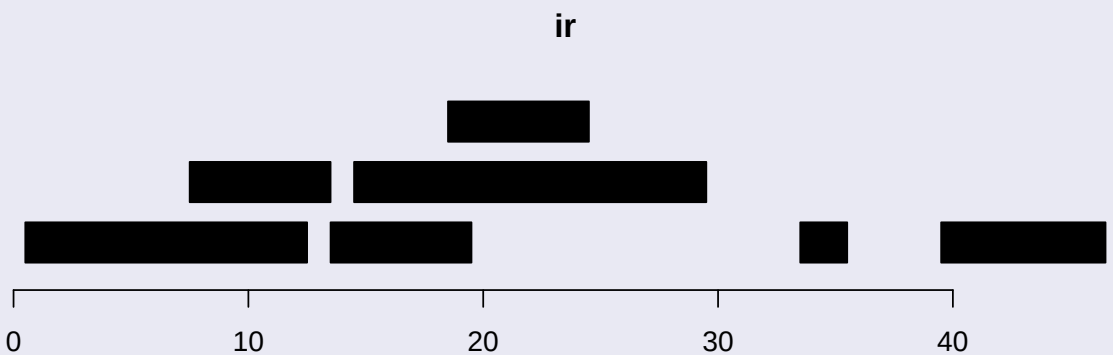
- Often interested in *consecutive* subsequences
- Consider the alphabet as a sequence:
  - {A, B, C} is a consecutive subsequence
  - The vowels would not be consecutive
- Compact representation: *range* (start and width)
- *Ranges* objects store a sequence of ranges

Creating a Ranges object

The *IRanges* class is a simple *Ranges* implementation.

Code

```
> ir <- IRanges(c(1, 8, 14, 15, 19, 34,
+     40), width = c(12, 6, 6, 15, 6, 2,
+     7))
```



Low level data access

Accessors

```
> start(ir)
[1]  1  8 14 15 19 34 40
> end(ir)
[1] 12 13 19 29 24 35 46
> width(ir)
[1] 12  6  6 15  6  2  7
```

Subsetting

Code

```
> ir[1:5]

IRanges of length 5
    start end width
[1]     1  12    12
[2]     8  13     6
[3]    14  19     6
[4]    15  29    15
[5]    19  24     6
```

Splitting up *Ranges* by sequence

Code

```
> rl <- split(ir, c(rep("chr1", 2), rep("chr2",
+     3), "chr1", "chr2"))
> rl[1]

CompressedIRangesList of length 1
$chr1
IRanges of length 3
    start end width
[1]     1  12    12
[2]     8  13     6
[3]    34  35     2
```

RangesList supports most *Ranges* operations, element-wise.

Shifting intervals

If your interval bounds are off by 1, you can shift them.

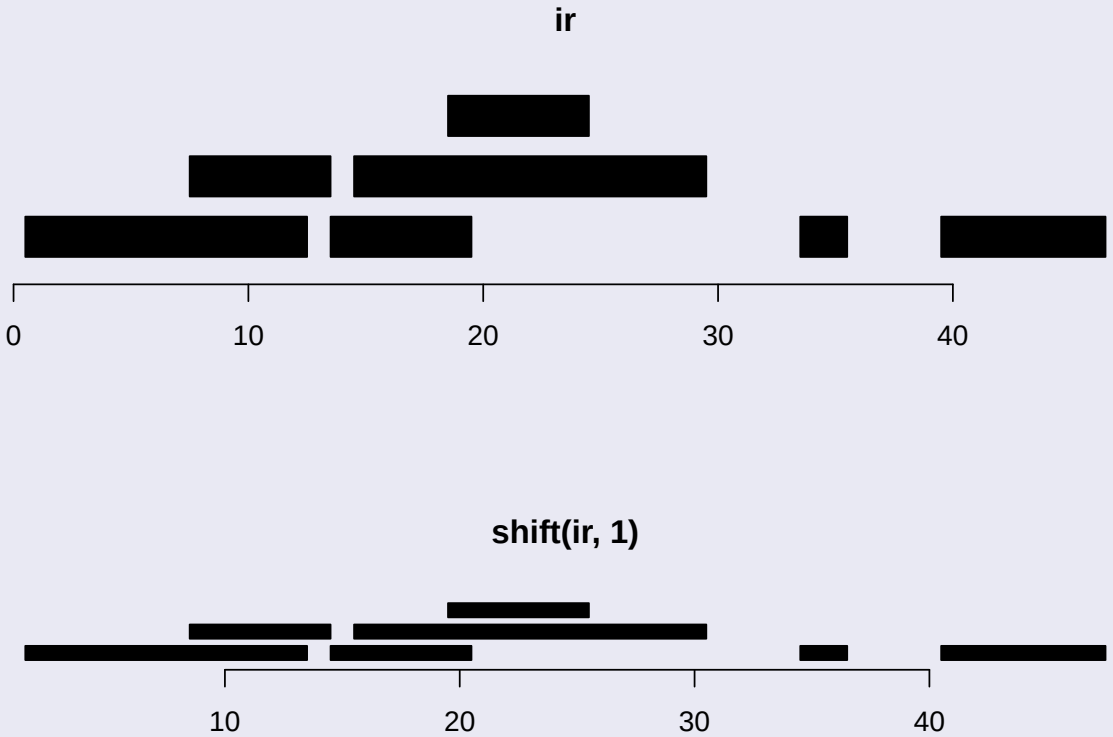
Code

```
> shift(ir, 1)
```

Shifting intervals

Code

```
> shift(ir, 1)
```



Resizing intervals

One common operation in ChIP-seq experiments is to "grow" an alignment interval to an estimated fragment length.

Code

```
> ir15 <- resize(ir, 15)
> print(ir15 <- resize(ir, 15, start = FALSE))

IRanges of length 7
    start end width
[1]    -2  12    15
[2]    -1  13    15
[3]     5  19    15
[4]    15  29    15
[5]    10  24    15
[6]    21  35    15
[7]    32  46    15
```

Restricting interval bounds

The previous operation created some negative start values. We can "clip" those negative values.

Code

```
> restrict(ir15, 1)

IRanges of length 7
    start end width
[1]     1  12    12
[2]     1  13    13
[3]     5  19    15
[4]    15  29    15
[5]    10  24    15
[6]    21  35    15
[7]    32  46    15
```

Normalizing ranges

- *Ranges* can represent a set of integers
- *NormalIRanges* formalizes this, with a compact, normalized representation
- `reduce` normalizes ranges

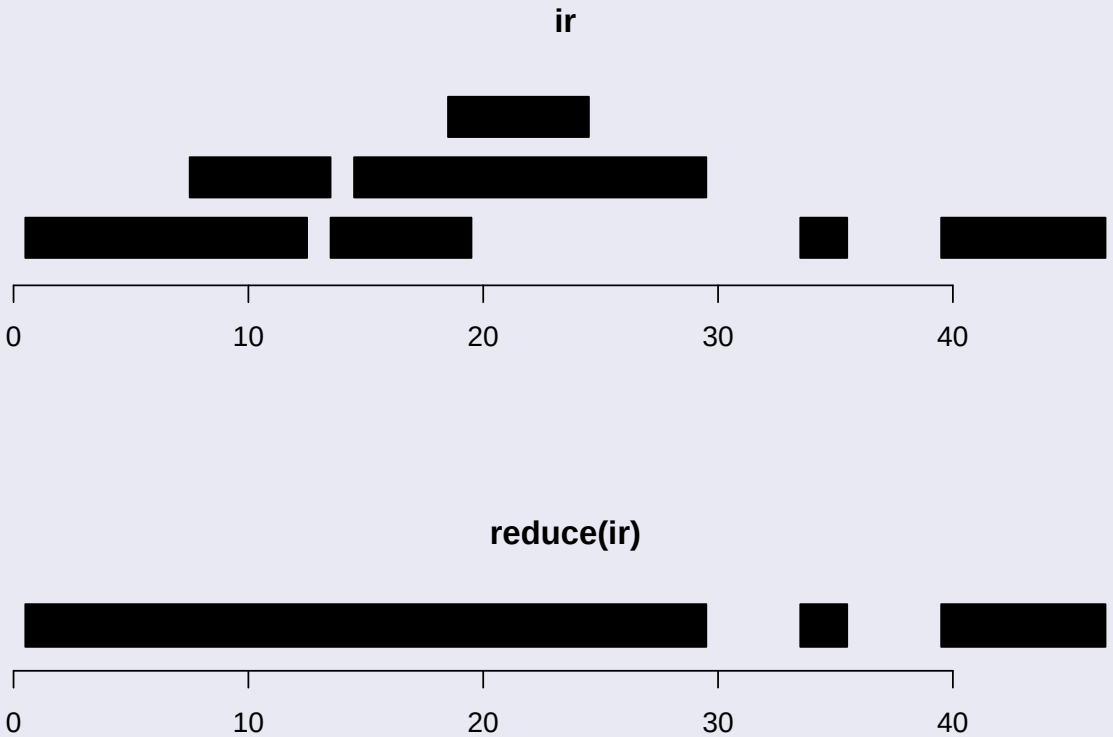
Code

```
> reduce(ir)
```

Normalizing ranges

Code

```
> reduce(ir)
```



Set operations

- *Ranges* as set of integers: `intersect`, `union`, `gaps`, `setdiff`
- Each range as integer set, in parallel: `pintersect`, `punion`, `pgap`, `psetdiff`

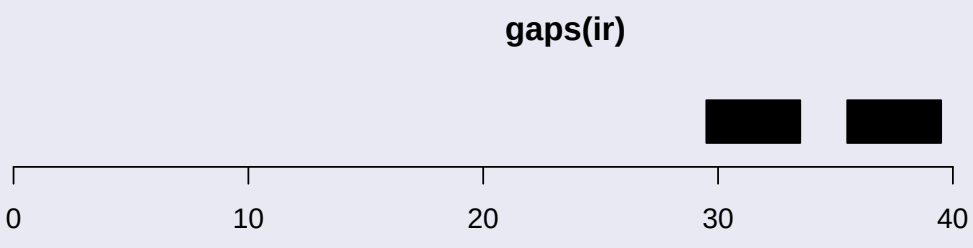
Example: `gaps`

```
> gaps(ir)
```

Set operations

Example: gaps

```
> gaps(ir)
```



Disjoining ranges

- Disjoint ranges are non-overlapping
- `disjoin` returns the widest ranges where the overlapping ranges are the same

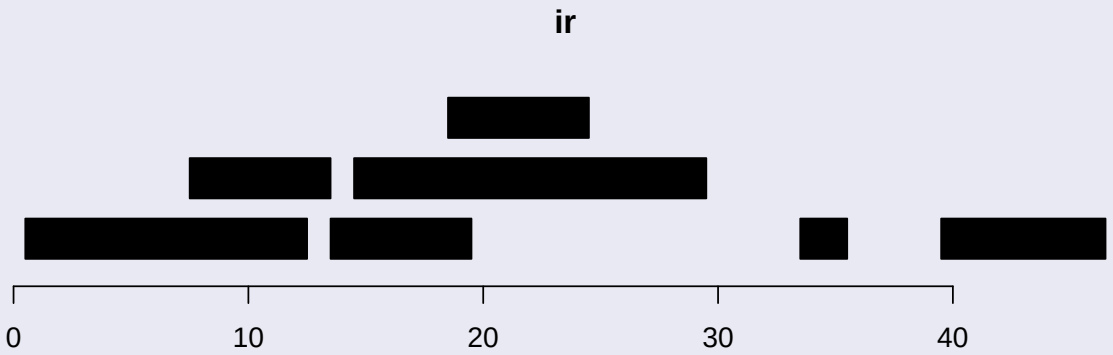
Code

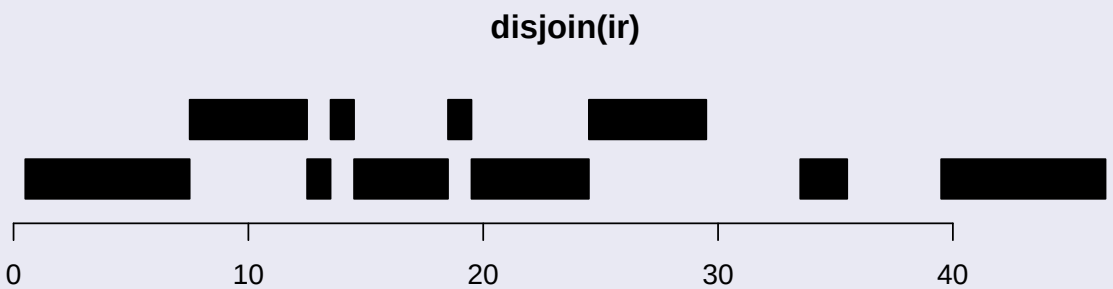
```
> disjoin(ir)
```

Disjoining ranges

Code

```
> disjoin(ir)
```





Overlap detection

- `overlap` detects overlaps between two *Ranges* objects
- Uses interval tree for efficiency

Code

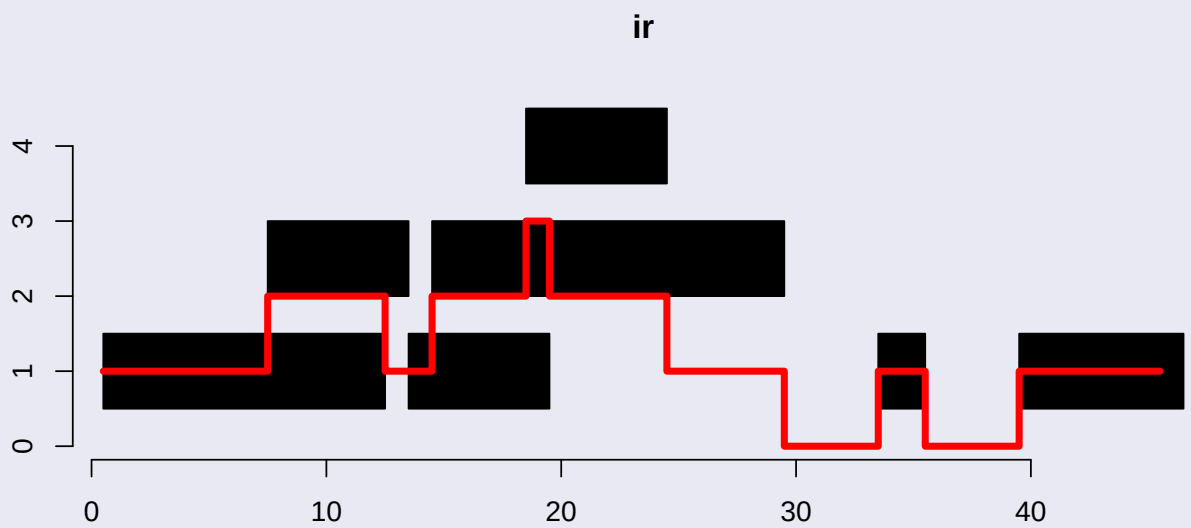
```
> ol <- findOverlaps(ir, reduce(ir))
> as.matrix(ol)

     query subject
[1,]     1       1
[2,]     2       1
[3,]     3       1
[4,]     4       1
[5,]     5       1
[6,]     6       2
[7,]     7       3
```

Counting overlapping Ranges

`coverage` counts number of ranges over each position

Code

```
> cov <- coverage(ir)
```



Coverage over **multiple** sequences

coverage also works for *RangesList*:

Code

```
> covL <- coverage(rl)
> covL

SimpleRleList of length 2
$chr1
'integer' Rle of length 35 with 5 runs
  Lengths:  7 5 1 20 2
  Values :  1 2 1 0 1

$chr2
'integer' Rle of length 46 with 8 runs
  Lengths:  13 1 4 1 5 5 10 7
  Values :  0 1 2 3 2 1 0 1
```

Finding nearest neighbors

- `nearest` finds the nearest neighbor ranges (overlapping is zero distance)
- `precede`, `follow` find non-overlapping nearest neighbors on specific side

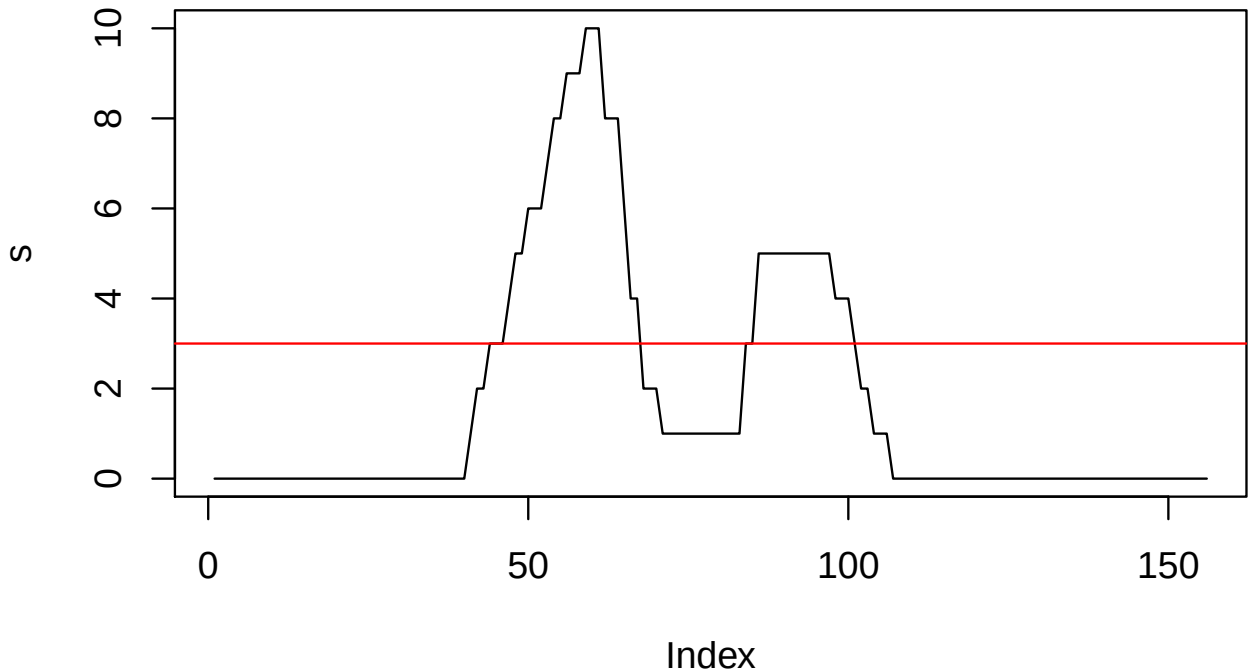
Outline

Ranges on Sequences: Views

- Associates a *Ranges* object with a sequence
- Sequences can be *Rle* or (in Biostrings) *XString*
- Extends *Ranges*, so supports the same operations

Slicing a Sequence into Views

Goal: find regions above cutoff of 3



Slicing a Sequence into Views

Goal: find regions above cutoff of 3

Using Rle

```
> Views(sRle, as(sRle > 3, "IRanges"))

Views on a 156-length Rle subject

views:
    start end width
[1]    47  67    21 [ 4  5  5  6  6  6  7 ...]
[2]    86 100    15 [5 5 5 5 5 5 5 5 5 5 5 ...]
```

Convenience

```
> sViews <- slice(sRle, 4)
```

Slicing **multiple** sequences into views

Like many *Rle* operations, `slice` also works on *RleList*.

Slicing a *RleList*

```
> sViewsList <- slice(sRleList, 4)
> sViewsList[1]

SimpleRleViewsList of length 1
$chr1
Views on a 78-length Rle subject

views:
    start end width
[1]    47  67    21 [ 4  5  5  6  6  6  7 ...]
```

Most *RleViews* methods also work on *RleViewsList*.

Summarizing windows

- Could `sapply` over each window
- Native functions available for common tasks: `viewMins`, `viewMaxs`, `viewSums`, ...

Sums

Maxima

Summarizing windows

- Could `sapply` over each window
- Native functions available for common tasks: `viewMins`, `viewMaxs`, `viewSums`, ...

Sums

```
> viewSums(sViews)

[1] 150  72

> viewSums(sViewsList)

SimpleNumericList of length 2
[["chr1"]] 150
[["chr2"]] 72
```

Maxima

Summarizing windows

- Could `sapply` over each window
- Native functions available for common tasks: `viewMins`, `viewMaxs`, `viewSums`, ...

Sums

Maxima

```
> viewMaxs(sViews)

[1] 10  5

> viewMaxs(sViewsList)

SimpleNumericList of length 2
[["chr1"]] 10
[["chr2"]] 5
```

Summarizing windows

- Could `sapply` over each window
- Native functions available for common tasks: `viewMins`, `viewMaxs`, `viewSums`, ...

Sums

Maxima

But how do we associate the summarized values with the original intervals?

Outline

Interval datasets

- Genomic coordinates consist of chromosome, position, and potentially strand information
- Each coordinate or set of coordinates may have additional values associated with it, such as GC content or alignment coverage
- A collection of intervals with data are commonly called tracks in genome browsers

Naive representation of interval dataset (1/2)

Tables in R are commonly stored in *data.frame* objects.

data.frame approach

```
> chr <- c("chr1", "chr2", "chr1")
> strand <- c("+", "+", "-")
> start <- c(3L, 4L, 1L)
> end <- c(7L, 5L, 3L)
> score <- c(1L, 3L, 2L)
> naiveTable <- data.frame(chr, strand,
+     score, start, end)
> naiveTable

   chr strand score start end
1 chr1      +     1     3   7
2 chr2      +     3     4   5
3 chr1      -     2     1   3
```

Naive representation of intervals with data row (2/2)

data.frame objects are poorly suited for this data because operations are constantly performed within chromosome/contig.

Using by to loop over data.frame

```
> getRange <- function(x) range(x[c("start",
+     "end")])
> by(naiveTable, naiveTable[["chr"]], getRange)

naiveTable[["chr"]]: chr1
[1] 1 7
------------------------------------
naiveTable[["chr"]]: chr2
[1] 4 5
```

RangedData construction

- Instances are created using the `RangedData` constructor.
- Interval starts and ends are wrapped in an *IRanges* constructor.
- Chromosome/contig information is supplied to `space` argument.

Code

```
> rdTable <- RangedData(IRanges(start, end),
+     strand, score, space = chr)
```

RangedData display

RangedData sacrifices row order flexibility for efficiency.

Code

```
> rdTable

RangedData with 3 rows and 2 value columns across 2 spaces
        space    ranges |      strand     score
  <character> <IRanges> | <character> <integer>
1        chr1    [3, 7] |           +         1
2        chr1    [1, 3] |           -         2
3        chr2    [4, 5] |           +         3
```

RangedData class decomposition

- *RangedData*
  - *RangesList* - intervals on chromosomes/contigs. Extracted using the `ranges` function.
    - *Ranges* - intervals for a specific chromosome/contig. Most common subclass is *IRanges*.
  - *SplitDataFrameList* - data on chromosomes/contigs. Extracted using the `values` function.
    - *DataFrame* - data for a specific chromosome/contig.

Primary accessors

Get the ranges

```
> ranges(rdTable)[1]

CompressedIRangesList of length 1
$chr1
IRanges of length 2
    start end width
[1]     3   7     5
[2]     1   3     3
```

Get the data values

Primary accessors

Get the ranges

Get the data values

```
> values(rdTable)[1]

CompressedSplitDataFrameList of length 1
$chr1
DataFrame with 2 rows and 2 columns
       strand     score
  <character> <integer>
1           +         1
2           -         2
```

Accessing built-in attributes

Each built-in feature attribute has a corresponding accessor method: `start`, `end`, `strand`, `chrom`, `genome`

Example

```
> start(rdTable)

[1] 3 1 4
```

Accessing data columns

Any data column (including strand) is accessible via `$` and `[[`.

Example

```
> rdTable$strand

[1] "+" "-" "+"
```

Overview of *RangedData* subsetting

- Often need to subset track features and data columns
- Example: limit the amount transferred to a genome browser
- Matrix style: `rd[i, j]`, where `i` is feature index and `j` is column index
- By chromosome: `rd[i]`, where `i` indexes the chromosome

Subsetting examples and exercises

Examples

```
> first10 <- rdTable[1:2, ]
> pos <- rdTable[rdTable$strand == "+",
+     ]
> chr1Table <- rdTable[1]
> scoreTable <- rdTable[, "score"]
```

Outline

Bridging the towers

Transitioning between *RleList* and *RangedData*

Various paths between piecewise constant measures (*Rle(List)*) and interval datasets (*RangedData*)

Rle(List) to *RangedData*

Via *RleViews(List)*

RangedData to *Rle(List)*

Bridging the towers

Transitioning between *RleList* and *RangedData*

Rle(List) to *RangedData*

```
> head(as(sRleList, "RangedData"), 3)

RangedData with 3 rows and 1 value column across 2 spaces
        space    ranges |     score
  <character> <IRanges> | <numeric>
1        chr1  [ 1, 40] |         0
2        chr1  [41, 41] |         1
3        chr1  [42, 43] |         2
```

Via *RleViews(List)*

RangedData to *Rle(List)*

Bridging the towers

Transitioning between *RleList* and *RangedData*

Rle(List) to *RangedData*

Via *RleViews(List)*

```
> height <- unlist(viewMaxs(sViewsList))
> RangedData(sViewsList, height)

RangedData with 2 rows and 1 value column across 2 spaces
        space    ranges |    height
  <character> <IRanges> | <numeric>
1        chr1  [47, 67] |        10
2        chr2  [ 8, 22] |         5
```

RangedData to *Rle(List)*

Bridging the towers

Transitioning between *RleList* and *RangedData*

Rle(List) to *RangedData*

Via *RleViews(List)*

RangedData to *Rle(List)*

```
> coverage(rdTable, weight = "score")[1]

SimpleRleList of length 1
$chr1
'integer' Rle of length 7 with 3 runs
  Lengths:  2 1 4
  Values :  2 3 1
```

Final Comments

- Just scratching the surface – much more under the hood. Exploration is encouraged.
- Trying to work around performance issues in R, but not entirely successful.
- Still in active development. Missing features or performance problems, let us know.