PeakSegDisk usage examples

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Welcome to PeakSegDisk, an R package for optimal peak detection in very large count data sequences.

1 Related work

The PeakSeg R packages contain algorithms for inferring optimal segmentation models subject to the constraint that up changes must be followed by down changes, and vice versa. This ensures that the model can be interpreted in terms of peaks (after up changes) and background (after down changes).

- PeakSegDP the historically first PeakSeg package, https://CRAN.R-project.org/package=PeakSegDP provides a heuristic quadratic time algorithm for computing models from 1 to S segments for a single sample. This was the original algorithm described in our ICML'15 paper, http://jmlr.org/proceedings/papers/v37/hocking15.html, but it is neither fast nor optimal, so in practice we recommend to use our newer packages below instead.
- PeakSegOptimal https://CRAN.R-project.org/package=PeakSegOptimal provides log-linear time algorithms for computing optimal models with multiple peaks for a single sample. The algorithms are faster and more accurate than PeakSegDP, https://arxiv.org/abs/1703.03352
- PeakSegDisk https://github.com/tdhock/PeakSegDisk provides an on-disk implementation of optimal log-linear algorithms for computing multiple peaks in a single sample. Computes same models as PeakSegOptimal but works for much larger data sets because disk is used for storage instead of memory. https://arxiv.org/abs/1810.00117
- PeakSegJoint https://CRAN.R-project.org/package=PeakSegJoint provides a fast heuristic algorithm for computing models with a single common peak in 0, ..., S samples. https://arxiv.org/abs/1506.01286
- PeakSegPipeline https://github.com/tdhock/PeakSegPipeline provides a pipeline for genome-wide peak calling using the other PeakSeg packages.

The remainder of this vignette is dedicated to an explanation of how to use PeakSegDisk.

2 Simulate a noisy integer vector with changes

The first example we will treat is detecting peaks in a vector of integer data, with possibly the same values at adjacent positions. This is an inefficient representation for large genomic data, but it is the typical output from simulation functions like rpois:

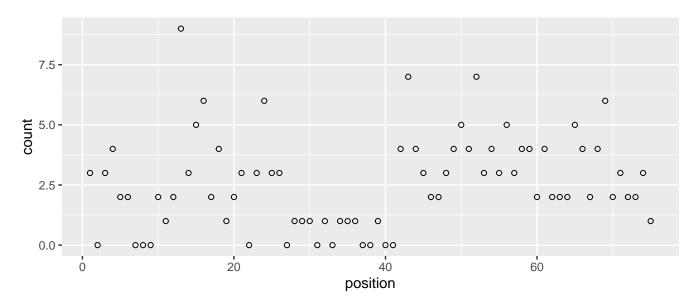
```
sim.seg <- function(seg.mean, size.mean=15){
    seg.size <- rpois(1, size.mean)
    rpois(seg.size, seg.mean)
}
set.seed(1)
seg.mean.vec <- c(1.5, 3.5, 0.5, 4.5, 2.5)
z.list <- lapply(seg.mean.vec, sim.seg)
(z.rep.vec <- unlist(z.list))

#> [1] 3 0 3 4 2 2 0 0 0 2 1 2 9 3 5 6 2 4 1 2 3 0 3 6 3 3 0 1 1 1 0 1 0 1 1 1 0 0
#> [39] 1 0 0 4 7 4 3 2 2 3 4 5 4 7 3 4 3 5 3 4 4 2 4 2 2 2 5 4 2 4 6 2 3 2 2 3 1
```

From the output above it is clear that these simulated data are integers, with some identical values at adjacent positions.

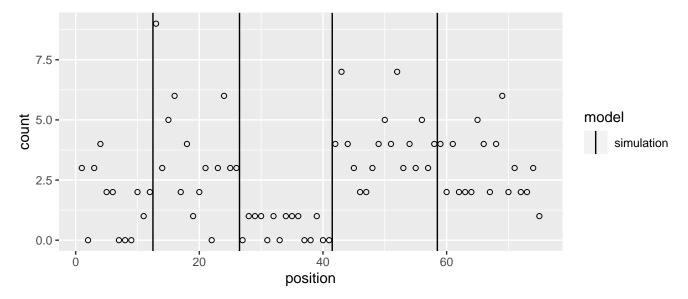
Below we put these data into a data table in order to plot them along with the model using ggplot2:

```
count.df <- data.frame(
   chrom="chrUnknown",
   chromStart=0:(length(z.rep.vec)-1),
   chromEnd=1:length(z.rep.vec),
   count=z.rep.vec)
library(ggplot2)
gg.count <- ggplot()+
   xlab("position")+
   geom_point(aes(
        chromEnd, count),
        shape=1,
        data=count.df)
gg.count</pre>
```



The true changepoints in the simulation are shown below.

```
n.segs <- length(seg.mean.vec)
seg.size.vec <- sapply(z.list, length)
seg.end.vec <- cumsum(seg.size.vec)
change.vec <- seg.end.vec[-n.segs]+0.5
change.df <- data.frame(
    changepoint=change.vec)
gg.change <- gg.count+
    geom_vline(aes(
        xintercept=changepoint, color=model),
        data=data.frame(change.df, model="simulation"))+
scale_color_manual(
    values=c(
        simulation="black",
        fitted="green"))
gg.change</pre>
```



3 Segment a vector of integers

Let $z_1, \ldots, z_n \in \mathbb{Z}_+$ be the sequence of n non-negative count data in z.rep.vec, and let $w_1 = \cdots = w_n = 1$ be weights which are all 1. The peak detection algorithm computes the solution to the following optimization problem:

where $\ell(m, z) = m - z \log m$ is the Poisson loss. The optimization variables are m_i for the segment mean, s_i for hidden state, and c_i for type of changepoint. The penalty term is proportional to the number of changepoint variables c_i which are equal to 1 (which is the same as the number of peaks in the resulting model).

To run the peak detection algorithm a numeric penalty parameter $\lambda \geq 0$ must be specified by the user. The smallest value is 0 which yields max peaks, and the largest value is Inf which yields no peaks. The code below runs the peak detection algorithm on this count data vector, using the penalty parameter $\lambda = 10.5$:

```
fit <- list()
(fit$vec <- PeakSegDisk::PeakSegFPOP_vec(z.rep.vec, 10.5))</pre>
#> $segments
#>
            chrom chromStart chromEnd
                                            status
                                                        mean
#> 1: chrUnknown
                           69
                                     75 background 2.166670
#> 2: chrUnknown
                                              peak 3.714290
                           41
#> 3: chrUnknown
                                     41 background 0.533333
                           26
#> 4: chrUnknown
                           12
                                     26
                                              peak 3.571430
#> 5: chrUnknown
                                     12 background 1.583330
                            0
#>
  $loss
#>
      penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
#>
                       5
                             2
#> 1:
         10.5
                                   75
                                                   60
                                                          0.01507491 -19.86938
      equality.constraints mean.intervals max.intervals megabytes seconds
#>
#> 1:
                           0
                                         4.6
                                                           8 0.01372147
                                                                           0.005
#>
#> $data
#>
             chrom chromStart chromEnd count
                                       1
#>
    1: chrUnknown
                             0
                                             3
                             1
                                       2
                                             0
#>
    2: chrUnknown
    3: chrUnknown
                             2
                                       3
                                             3
#>
                             3
    4: chrUnknown
                                       4
                                             4
#>
    5: chrUnknown
                             4
                                       6
                                             2
#>
    6: chrUnknown
                             6
                                       9
                                             0
                                             2
#>
    7: chrUnknown
                             9
                                      10
#>
    8: chrUnknown
                            10
                                      11
                                              1
    9: chrUnknown
                            11
                                      12
                                             2
#> 10: chrUnknown
                                             9
                            12
                                      13
#> 11: chrUnknown
                                             3
                            13
                                      14
#> 12: chrUnknown
                                             5
                            14
                                      15
#> 13: chrUnknown
                            15
                                      16
                                             6
                                             2
#> 14: chrUnknown
                            16
                                      17
#> 15: chrUnknown
                            17
                                             4
                                      18
#> 16: chrUnknown
                            18
                                      19
                                              1
                                             2
#> 17: chrUnknown
                            19
                                      20
#> 18: chrUnknown
                            20
                                      21
                                             3
#> 19: chrUnknown
                            21
                                      22
```

```
#> 20: chrUnknown
                            22
                                      23
                                              3
#> 21: chrUnknown
                            23
                                      24
                                              6
                                              3
#> 22: chrUnknown
                            24
                                      26
#> 23: chrUnknown
                                              0
                            26
                                      27
#> 24: chrUnknown
                            27
                                              1
                                      30
#> 25: chrUnknown
                            30
                                      31
                                              0
#> 26: chrUnknown
                            31
                                      32
                                              1
#> 27: chrUnknown
                            32
                                      33
                                              0
#> 28: chrUnknown
                            33
                                      36
                                              1
#> 29: chrUnknown
                            36
                                      38
                                              0
#> 30: chrUnknown
                            38
                                      39
                                              1
#> 31: chrUnknown
                            39
                                              0
                                      41
#> 32: chrUnknown
                            41
                                      42
                                              4
                                              7
#> 33: chrUnknown
                            42
                                      43
#> 34: chrUnknown
                            43
                                      44
                                              4
                                              3
#> 35: chrUnknown
                            44
                                      45
                                              2
#> 36: chrUnknown
                            45
                                      47
#> 37: chrUnknown
                                              3
                            47
                                      48
#> 38: chrUnknown
                            48
                                      49
                                              4
#> 39: chrUnknown
                            49
                                      50
                                              5
#> 40: chrUnknown
                                              4
                            50
                                      51
                                              7
#> 41: chrUnknown
                            51
                                      52
#> 42: chrUnknown
                            52
                                      53
                                              3
                                              4
#> 43: chrUnknown
                            53
                                      54
#> 44: chrUnknown
                            54
                                      55
                                              3
#> 45: chrUnknown
                                              5
                            55
                                      56
#> 46: chrUnknown
                            56
                                      57
                                              3
#> 47: chrUnknown
                            57
                                      59
                                              4
                                              2
#> 48: chrUnknown
                            59
                                      60
#> 49: chrUnknown
                                              4
                            60
                                      61
#> 50: chrUnknown
                            61
                                      64
                                              2
#> 51: chrUnknown
                                              5
                            64
                                      65
#> 52: chrUnknown
                            65
                                      66
                                              4
#> 53: chrUnknown
                            66
                                      67
                                              2
#> 54: chrUnknown
                            67
                                      68
                                              4
#> 55: chrUnknown
                            68
                                      69
                                              6
                                              2
#> 56: chrUnknown
                            69
                                      70
#> 57: chrUnknown
                            70
                                      71
                                              3
#> 58: chrUnknown
                            71
                                      73
                                              2
#> 59: chrUnknown
                            73
                                      74
                                              3
                                      75
                                              1
#> 60: chrUnknown
                            74
#>
             chrom chromStart chromEnd count
#>
#> attr(,"class")
#> [1] "PeakSegFPOP_df"
                           "PeakSegFPOP_dir" "list"
```

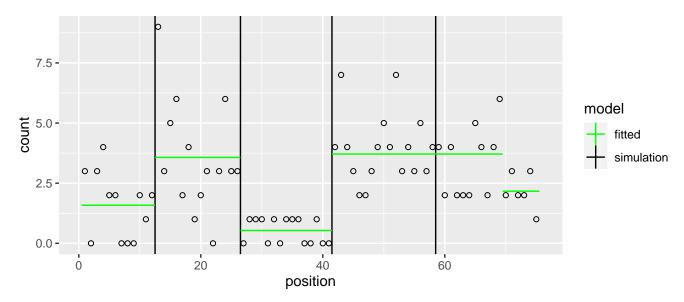
The model output list above includes segments, a data table with one row for each segment mean,

and loss, a data table with one row that reports the model meta-data. Of interest are:

- penalty, the user-provided penalty value,
- segments, the number of segments,
- peaks, the number of peaks (even-numbered segments),
- bases, the number of data points in repetitive form (not run-length encoding),
- bedGraph.lines, the number of data points in run-length encoding form,
- mean.pen.cost, the optimal mean loss plus penalty*peaks,
- total.loss, the optimal total Poisson loss over all data points,
- equality.constraints, the number of adjacent segment means that are equal in the optimal solution. Note that when this number is greater than 0, then there are some active equality constraints, and the optimal model is therefore not feasible for the strict inequality constraints, which implies that the optimum of the problem with strict inequality constraints is undefined, i.e. for any sub-optimal solution that satisfies the strict inequality constraints, we can find a lower cost solution that satisfies the strict inequality constraints (but is still sub-optimal), by getting closer to the solution with active equality constraints.
- megabytes, the storage space on disk used by the solver,
- seconds, the amount of time used by the solver,
- mean.intervals, max.intervals, statistics over all intervals (candidate changepoints) computed by the functional pruning algorithm, useful for analyzing computational complexity, which is linear in the number of intervals.

Note in particular that PeakSegFPOP_vec internally uses rle to construct a run-length encoding, which is passed to the solver to save time/storage. In this case the repetitive integer data vector contains 75 elements but the coverage.bedGraph data file contains only 60 lines. In real genomic data sets the difference is typically much larger.

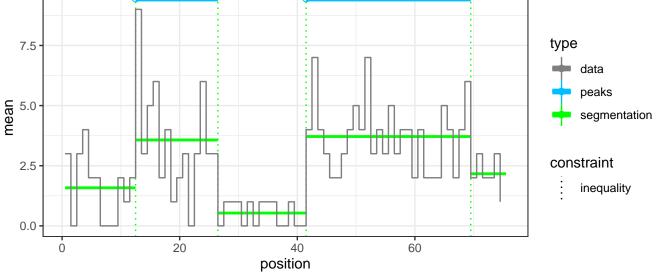
```
gg.change+
  geom_segment(aes(
    chromStart+0.5, mean, xend=chromEnd+0.5, yend=mean, color=model),
  data=data.frame(fit$vec$segments, model="fitted"))
```



It is clear from the plot above that the first three changepoints are estimated exactly and the last one is a bit over-estimated.

Also note that a default plot method is defined for these objects:

plot(fit\$vec)



4 Segment a data frame

Another interface that can be used on a data frame with n rows and exactly 4 columns (chrom, chrom-Start, chromEnd, count) is PeakSegFPOP_df. For each row $i \in \{1, ..., n\}$, let $z_i \in \mathbb{Z}_+$ be the non-negative count data (count column), and let $w_i > 0$ be the weight (equal to the number of bases, chromEnd-chromStart). The optimization problem we solve is the same as before. Note that this function does not perform run-length encoding for you:

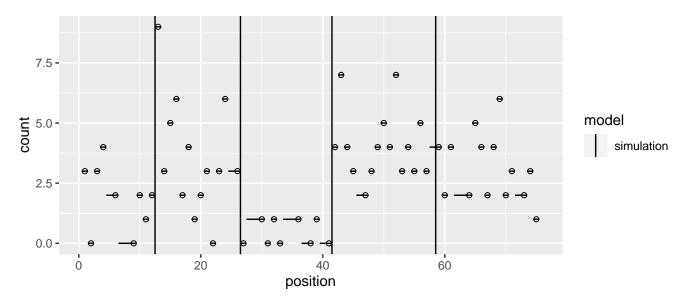
```
(fit$df <- PeakSegDisk::PeakSegFPOP_df(count.df, 10.5))</pre>
#> $segments
#>
          chrom chromStart chromEnd
                                        status
                                                  mean
#> 1: chrUnknown
                                 75 background 2.166670
                        69
#> 2: chrUnknown
                                    peak 3.714290
                        41
#> 3: chrUnknown
                        26
                                41 background 0.533333
#> 4: chrUnknown
                        12
                                26
                                        peak 3.571430
#> 5: chrUnknown
                       0
                                12 background 1.583330
#>
#> $loss
     penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
#> 1: 10.5 5 2 75 75 0.01507491 -19.86938
     equality.constraints mean.intervals max.intervals megabytes seconds
                                             8 0.01725006
#> 1:
                        0
                               4.633333
#>
#> $data
#>
           chrom chromStart chromEnd count
   1: chrUnknown
                          ()
   2: chrUnknown
                                   2
#>
                          1
                                         0
                         2
#>
  3: chrUnknown
                                   3
#> 4: chrUnknown
                         3
                                   4
                         4
                                   5
#> 5: chrUnknown
#> 6: chrUnknown
                         5
                                   6
#> 7: chrUnknown
                         6
                                   7
                                        0
                         7
#> 8: chrUnknown
                                  8
#> 9: chrUnknown
                         8
                                   9
                                         0
#> 10: chrUnknown
                         9
                                  10
#> 11: chrUnknown
                                         1
                        10
                                  11
#> 12: chrUnknown
                        11
                                  12
#> 13: chrUnknown
                                         9
                        12
                                  13
#> 14: chrUnknown
                        13
                                  14
#> 15: chrUnknown
                        14
                                  15
                                         5
#> 16: chrUnknown
                        15
                                  16
#> 17: chrUnknown
                        16
                                  17
                                         2
#> 18: chrUnknown
                         17
                                  18
                                        4
#> 19: chrUnknown
                        18
                                  19
                                         1
#> 20: chrUnknown
                                         2
                        19
                                  20
#> 21: chrUnknown
                         20
                                  21
                                         3
#> 22: chrUnknown
                         21
                                  22
                                         0
#> 23: chrUnknown
                         22
                                  23
                                         3
#> 24: chrUnknown
                         23
                                  24
                                         6
                                         3
#> 25: chrUnknown
                         24
                                  25
#> 26: chrUnknown
                         25
                                         3
                                  26
#> 27: chrUnknown
                         26
                                  2.7
                                         0
#> 28: chrUnknown
                         27
                                  28
                                         1
#> 29: chrUnknown
                         28
                                  29
```

#>	30:	chrUnknown	29	30	1
#>	31:	chrUnknown	30	31	0
#>	32:	chrUnknown	31	32	1
#>	33:	chrUnknown	32	33	0
#>	34:	chrUnknown	33	34	1
#>	35:	chrUnknown	34	35	1
#>		chrUnknown	35	36	1
#>		chrUnknown	36	37	0
#>		chrUnknown	37	38	
		chrUnknown	38	39	0
#>					1
		chrUnknown	39	40	0
#>		chrUnknown	40	41	0
		chrUnknown	41	42	4
		chrUnknown	42	43	7
#>	44:	chrUnknown	43	44	4
#>	45:	chrUnknown	44	45	3
#>	46:	chrUnknown	45	46	2
#>	47:	chrUnknown	46	47	2
#>	48:	chrUnknown	47	48	3
		chrUnknown	48	49	4
#>		chrUnknown	49	50	5
#>		chrUnknown	50	51	4
#>		chrUnknown	51	52	7
#>		chrUnknown	52	53	3
#>		chrUnknown	53	54	4
#>		chrUnknown	54	55	3
#>		chrUnknown	55	56	5
#>		chrUnknown	56	57	3
#>		chrUnknown	57	58	4
#>	59:	chrUnknown	58	59	4
#>	60:	chrUnknown	59	60	2
#>	61:	chrUnknown	60	61	4
#>	62:	chrUnknown	61	62	2
		chrUnknown	62	63	2
		chrUnknown	63	64	2
		chrUnknown	64	65	5
		chrUnknown	65	66	4
		chrUnknown	66	67	2
		chrUnknown	67	68	4
		chrUnknown	68	69	6
		chrUnknown	69	70	2
#>	71:	chrUnknown	70	71	3
#>	72:	chrUnknown	71	72	2
#>	73:	chrUnknown	72	73	2
#>	74:	chrUnknown	73	74	3
#>	75:	chrUnknown	74	75	1

```
#> chrom chromStart chromEnd count
#>
#> attr(,"class")
#> [1] "PeakSegFPOP_df" "PeakSegFPOP_dir" "list"
```

Note how bedGraph.lines is now the same size as bases, 75. The time/storage complexity is log-linear in the number of bedGraph.lines, so it is more efficient to use the run-length encoding. This can be easily done in R:

```
z.rle.vec <- rle(z.rep.vec)</pre>
chromEnd <- cumsum(z.rle.vec$lengths)</pre>
rle.df <- data.frame(</pre>
  chrom="chrUnknown",
  chromStart=c(OL, chromEnd[-length(chromEnd)]),
  chromEnd,
  count=z.rle.vec$values)
gg.rle <- ggplot()+
  geom_segment(aes(
    chromStart+0.5, count, xend=chromEnd+0.5, yend=count),
    data=rle.df)+
  geom_point(aes(
    chromEnd, count),
    shape=1,
    data=rle.df)+
  geom_vline(aes(
    xintercept=changepoint, color=model),
    data=data.frame(change.df, model="simulation"))+
  scale_color_manual(
    values=c(
      simulation="black",
      fitted="green"))+
  xlab("position")
gg.rle
```

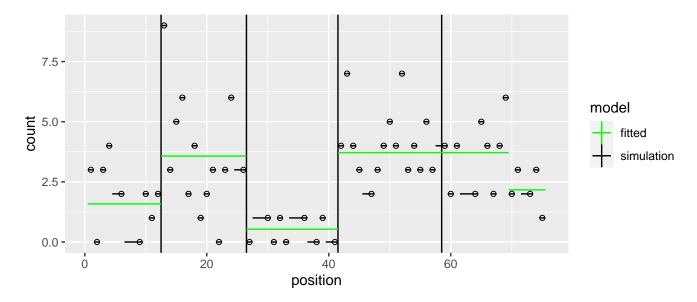


The plot above shows the run-length encoded data, with a geom_point for the last position in each run, and a geom_segment extending left to the first position. These data can be segmented as above:

```
(fit$rle <- PeakSegDisk::PeakSegFPOP_df(rle.df, 10.5))</pre>
#> $segments
#>
            chrom chromStart chromEnd
                                            status
                                                        mean
#> 1: chrUnknown
                           69
                                     75 background 2.166670
  2: chrUnknown
                           41
                                     69
                                              peak 3.714290
#> 3: chrUnknown
                           26
                                     41 background 0.533333
  4: chrUnknown
                           12
                                     26
                                              peak 3.571430
  5: chrUnknown
                            0
                                     12 background 1.583330
#>
  $loss
#>
#>
      penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
         10.5
                      5
                             2
                                                          0.01507491 -19.86938
  1:
                                  75
                                                   60
      equality.constraints mean.intervals max.intervals
                                                            megabytes seconds
#>
                           0
                                         4.6
                                                           8 0.01372147
  1:
                                                                           0.004
#>
#>
  $data
             chrom chromStart chromEnd count
#>
#>
    1: chrUnknown
                             0
                                       1
                                             3
    2: chrUnknown
                             1
                                       2
                                             0
#>
    3: chrUnknown
                             2
                                       3
                                              3
#>
    4: chrUnknown
                             3
                                       4
                                             4
#>
#>
    5: chrUnknown
                             4
                                       6
                                             2
                             6
                                       9
                                             0
#>
    6: chrUnknown
                                             2
    7: chrUnknown
                             9
                                      10
#>
                            10
                                              1
#>
    8: chrUnknown
                                      11
                                             2
    9: chrUnknown
                            11
                                      12
  10: chrUnknown
                            12
                                      13
                                             9
#> 11: chrUnknown
                            13
                                      14
```

12: chrUnknown					
14: chrUnknown	C	chrUnknown	14	15	ĺ
15	C	chrUnknown	15	16	(
16: chrUnknown	C	chrUnknown	16	17	4
17: chrUnknown 19	C	chrUnknown	17	18	4
18: chrUnknown 20	C	chrUnknown	18	19	
19: chrUnknown 21 22 23 20: chrUnknown 22 23 24 26 27 22 24 26 27 24 26 27 24 26 27 24 26 27 30 24 26 27 30 25 25 25 25 25 25 25 2	C	chrUnknown	19	20	2
19: chrUnknown 21 22 23 20: chrUnknown 22 23 24 26 27 22 24 26 27 24 26 27 24 26 27 24 26 27 30 24 26 27 30 25 25 25 25 25 25 25 2					3
22 23 24 21: chrUnknown 23 24 26 22: chrUnknown 24 26 27 22: chrUnknown 26 27 30 24: chrUnknown 26 27 30 24: chrUnknown 27 30 31 22: chrUnknown 30 31 32 25: chrUnknown 31 32 33 22: chrUnknown 31 32 33 36 22: chrUnknown 32 33 36 22: chrUnknown 36 38 39 28: chrUnknown 36 38 39 31: chrUnknown 39 41 42 33: chrUnknown 41 42 43 32: chrUnknown 41 42 43 33: chrUnknown 42 43 44 25 35: chrUnknown 45 47 48 36: chrUnknown 45 47 48 39: chrUnknown 47 48 49 39: chrUnknown 49 50 51 52 53 54: chrUnknown 51 52 53 43: chrUnknown 51 52 53 43: chrUnknown 51 52 53 44: chrUnknown 51 52 53 44: chrUnknown 51 52 53 45: chrUnknown 51 52 53 55: chrUnknown 51 55 56 56 57 47: chrUnknown 57 59 58 48: chrUnknown 57 59 58 48: chrUnknown 57 59 58 55: chrUnknown 66 67 55: chrUnknown 67 68 69					(
221: chrUnknown 24 26 222: chrUnknown 24 26 23: chrUnknown 26 27 24: chrUnknown 27 30 25: 25: chrUnknown 30 31 26: 25: chrUnknown 31 32 27: chrUnknown 32 33 28: chrUnknown 36 38 29: chrUnknown 36 38 29: chrUnknown 39 41 20: 33: chrUnknown 41 42 21: chrUnknown 42 43 22: chrUnknown 43 44 23: chrUnknown 44 45 24: chrUnknown 45 47 25: chrUnknown 46 47 26: 27: chrUnknown 39 41 27: chrUnknown 39 41 28: chrUnknown 39 41 29: chrUnknown 41 42 20: 20: chrUnknown 42 43 20: 20: chrUnknown 44 45 20: 20: chrUnknown 45 47 20: 20: chrUnknown 46 47 20: 20: chrUnknown 47 21: chrUnknown 48 22: chrUnknown 49 23: chrUnknown 49 24: chrUnknown 49 25: chrUnknown 49 26: 27 27 28 29: chrUnknown 30 20: 20: 20: 20: 20: 20: 20: 20: 20: 20:					3
22: chrUnknown 26 27 30 24: chrUnknown 26 27 30 24: chrUnknown 27 30 31 32 25: chrUnknown 31 32 33 36 26: chrUnknown 32 33 36 28: chrUnknown 36 38 39 30: chrUnknown 39 41 42 33: chrUnknown 41 42 43 34: chrUnknown 42 43 34: chrUnknown 45 47 48 36: chrUnknown 47 48 49 39: chrUnknown 48 49 39: chrUnknown 49 50 51 52 53 56 57 47: chrUnknown 57 59 48: chrUnknown 57 59 48: chrUnknown 57 59 49: chrUnknown 50 51: chrUnknown 57 59 54: chrUnknown 57 66 57 54: chrUnknown 66 67 55: chrUnknown 67 68 69					(
223: chrUnknown 26 27 30 24: chrUnknown 27 30 31 25: chrUnknown 31 32 33 36 26: chrUnknown 32 33 36 28: chrUnknown 36 38 39 30: chrUnknown 39 41 42 33: chrUnknown 41 42 43 34: chrUnknown 45 47 35: chrUnknown 45 47 48 36: chrUnknown 47 48 49 39: chrUnknown 49 50 40: chrUnknown 50 51 52 42: chrUnknown 50 51 52 42: chrUnknown 50 51 52 44: chrUnknown 50 51 52 53 54 54: chrUnknown 50 56 57 56 55: chrUnknown 50 66 57 55: chrUnknown 50 66 57 55: chrUnknown 66 67 55: chrUnknown 67 68 69					3
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	C	chrUnknown	69	70	6
> 57: chrUnknown 70 71	C	chrUnknown	70	71	3

```
58: chrUnknown
                                    73
  59: chrUnknown
                           73
                                    74
                                            3
   60: chrUnknown
                           74
                                    75
                                            1
            chrom chromStart chromEnd count
#>
#>
  attr(,"class")
  [1] "PeakSegFPOP_df"
                          "PeakSegFPOP_dir" "list"
gg.rle+
  geom_segment(aes(
    chromStart+0.5, mean, xend=chromEnd+0.5, yend=mean, color=model),
    data=data.frame(fit$rle$segments, model="fitted"))
```



5 Write the file yourself

The interfaces discussed in the previous sections are perhaps the most intuitive for useRs, but they are also the least efficient, so they are not recommended for large data.

In this section we introduce the most efficient way of using PeakSegDisk, which involves:

- creating a "problem" directory for each segmentation problem (sample and genome subset),
- saving the data to coverage.bedGraph in that directory,
- and then running PeakSegFPOP_dir.

The reason why this method is recommended for large data is because PeakSegFPOP_dir saves its results to the "problem" directory. So if a certain result has already been computed, these result files are used as a cache, and are read instead of doing computations, which saves a lot of time. The file system is used as the interface in order to support very large data sets with very little memory usage.

To use PeakSegFPOP_dir the data should be saved to a chrXX-start-end/coverage.bedGraph file, where the problem directory "chrXX-start-end" should be named using a genome postion string:

- chrXX is the chromosome (which is irrelevant to the algorithm),
- start is the 0-based first position of the region to segment (the smallest possible value is 0),
- end is the 1-based end position (the smallest possible value is 1).

```
data.dir <- file.path(
   tempfile(),
   with(rle.df, sprintf(
      "%s-%d-%d", chrom[1], min(chromStart), max(chromEnd))))
dir.create(data.dir, showWarnings=FALSE, recursive=TRUE)
coverage.bedGraph <- file.path(data.dir, "coverage.bedGraph")
write.table(
   rle.df, coverage.bedGraph,
   sep="\t", row.names=FALSE, col.names=FALSE)</pre>
```

The next step is to run the main solver,

```
(fit$dir <- PeakSegDisk::PeakSegFPOP_dir(data.dir, 10.5))
#> $segments
#>
           chrom chromStart chromEnd
                                          status
                                                      mean
                                   75 background 2.166670
#> 1: chrUnknown
                          69
#> 2: chrUnknown
                                            peak 3.714290
                          41
#> 3: chrUnknown
                                   41 background 0.533333
                          26
#> 4: chrUnknown
                                            peak 3.571430
                          12
                                   26
#> 5: chrUnknown
                           0
                                   12 background 1.583330
#>
#> $loss
      penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
                     5
                            2
         10.5
                                 75
                                                 60
                                                       0.01507491 -19.86938
#> 1:
#>
      equality.constraints mean.intervals max.intervals megabytes seconds
                                                        8 0.01372147
#> 1:
                                       4.6
                                                                        0.004
                          0
#>
#> attr(,"class")
#> [1] "PeakSegFPOP_dir" "list"
```

The underlying C++ code creates penalty-specific files such as

chrXX-start-end/coverage.bedGraph_penalty=0.1_loss.tsv which are used to store/cache the results. If the files already exist (and are consistent) then PeakSegFPOP_dir just reads them; otherwise it runs the dynamic programming C++ code in order to create those files, which are then read into R.

6 Computing the model with a given number of peaks

The **sequentialSearch_dir** function can be used to compute the optimal model with a certain number of peaks:

```
if(interactive() && requireNamespace("future"))future::plan("multiprocess")
(fit$search <- PeakSegDisk::sequentialSearch_dir(data.dir, 2L, verbose=1))</pre>
#> Loading required namespace: future.apply
\#> Next = 0, Inf
#> Next = 2.20991803112367
\# Next = 7.11950550040458
#> $segments
#>
           chrom chromStart chromEnd
                                           status
                                                      mean
#> 1: chrUnknown
                          69
                                   75 background 2.166670
#> 2: chrUnknown
                                             peak 3.714290
                          41
                                   69
#> 3: chrUnknown
                                   41 background 0.533333
                          26
#> 4: chrUnknown
                          12
                                   26
                                             peak 3.571430
                                   12 background 1.583330
#> 5: chrUnknown
                           0
#>
#> $loss
       penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
#> 1: 7.119506
                                                       -0.07507161 -19.86938
                       5
                             2
                                  75
                                                  60
      equality.constraints mean.intervals max.intervals megabytes seconds
                                  4.558333
                                                         9 0.0136261
#> 1:
                          0
                                                                       0.004
#>
      iteration under over
              3
                     0
#> 1:
#>
#> $others
       penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
#> 1: 0.000000
                      53
                            26
                                  75
                                                  60
                                                       -0.63772877 -47.829658
#> 2:
                      1
                             0
           Inf
                                  75
                                                  60
                                                         0.12837615
                                                                      9.628211
#> 3: 2.209918
                      13
                             6
                                  75
                                                       -0.26439085 -33.088822
                                                  60
#> 4: 7.119506
                             2
                                  75
                                                       -0.07507161 -19.869382
                       5
                                                  60
#>
      equality.constraints mean.intervals max.intervals
                                                             megabytes seconds
#> 1:
                          5
                                  2.550000
                                                         4 0.009029388
                                                                         0.004
#> 2:
                          0
                                  0.000000
                                                         0 0.000000000
                                                                         0.001
#> 3:
                          0
                                  4.708333
                                                        9 0.013969421
                                                                         0.004
                                  4.558333
                                                         9 0.013626099
                                                                         0.004
      iteration under over
#>
#> 1:
                   NA
#> 2:
              1
                   NA
                         NA
              2
                     0
#> 3:
                         26
#> 4:
              3
                     0
                          6
#>
#> attr(,"class")
#> [1] "PeakSegFPOP_dir" "list"
```

The algorithm must evaluate several penalty values to compute the optimal model with a certain number of peaks. The others component of the model list above shows that

• the search starts with penalty values 0 and Inf, which result in models with 26 and 0 peaks,

respectively.

- the next penalty evaluated is 2.21, which results in 6 peaks.
- the final penalty evaluated is 7.12, which results in 2 peaks.

At each step (except the first) the new penalties are computed based on the loss values found in the previous step. If present with a registered parallel future plan, the future.apply package is used to run the first step (penalties $0, \infty$) in parallel.

Note how the number of peaks and total.loss of this model is the same as the other models computed above,

```
lossDF <- function(L)data.frame(L$loss)[, names(fit$dir$loss)]</pre>
do.call(rbind, lapply(fit, lossDF))
#>
             penalty segments peaks bases bedGraph.lines mean.pen.cost total.loss
           10.500000
                             5
                                   2
                                                                0.01507491
#> vec
                                         75
                                                         60
                                                                             -19.86938
#> df
          10.500000
                             5
                                   2
                                         75
                                                         75
                                                                0.01507491
                                                                            -19.86938
#> rle
          10.500000
                             5
                                   2
                                         75
                                                                            -19.86938
                                                         60
                                                                0.01507491
#> dir
          10.500000
                             5
                                   2
                                         75
                                                         60
                                                                0.01507491
                                                                             -19.86938
                             5
                                   2
                                         75
#> search 7.119506
                                                         60
                                                               -0.07507161
                                                                             -19.86938
#>
           equality.constraints mean.intervals max.intervals
                                                                  megabytes seconds
                                                               8 0.01372147
#> vec
                               0
                                        4.600000
                                                                               0.005
                                        4.633333
                                                               8 0.01725006
#> df
                               0
                                                                               0.005
                               0
                                        4.600000
                                                               8 0.01372147
#> rle
                                                                               0.004
#> dir
                               0
                                        4.600000
                                                               8 0.01372147
                                                                               0.004
#> search
                               0
                                        4.558333
                                                               9 0.01362610
                                                                               0.004
```

Finally we demonstrate how the filesystem caching is especially useful for the sequential search. In the code below we ask the sequential search algorithm to compute the optimal model with four peaks:

```
four.peaks <- PeakSegDisk::sequentialSearch_dir(data.dir, 4L)</pre>
four.peaks$others[, .(iteration, penalty, peaks)]
                 penalty peaks
#>
      iteration
#> 1:
               1 0.000000
                               26
#> 2:
               1
                                0
                       Inf
#> 3:
               2 2.209918
                                6
               3 7.119506
                                2
#> 4:
               4 3.304860
                                3
#> 5:
#> 6:
               5 2.830674
                                5
#> 7:
               6 3.107790
                                4
```

Looking at the output above, we see that the first three iterations of the sequential search require computing models with 26, 0, 6, 2 peaks. Since all of these have been previously computed (and saved to disk), the dynamic programming algorithm does not need to be re-run, and instead the model results are simply read from the files. After that the dynamic programming is run for the subsequent iterations 4-6. In this particular example the savings in computation time is not extraordinary, but in real genomic data, this can result in substantial speed-ups.