Software Manual
Institute of Bioinformatics, Johannes Kepler University Linz

fastseg

An R Package for fast segmentation

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Scope and Purpose of this Document

This document is a user manual for the R package `fastseg`. It is only meant as a gentle introduction into how to use the basic functions implemented in this package. Not all features of the R package are described in full detail. Such details can be obtained from the documentation enclosed in the R package. Further note the following: (1) this is neither an introduction to segmentation algorithms; (2) this is not an introduction to R. If you lack the background for understanding this manual, you first have to read introductory literature on these subjects.

Contents

1 Introduction

fastseg implements a very fast and efficient segmentation algorithm. It has similar functionality as DNACopy (Olshen et al., 2004) but is considerably faster and more flexible. fastseg can segment data stemming from DNA microarrays and data stemming from next generation sequencing for example to detect copy number segments. Further it can segment data stemming from RNA microarrays like tiling arrays to identify transcripts. Most generally, it can segment data given as a matrix or as a vector. Various data formats can be used as input to fastseg like expression set objects for microarrays or GRanges for sequencing data.

The segmentation criterion of fastseg is based on a statistical test in a Bayesian framework, namely the cyber t-test (Baldi and Long, 2001). The speed-up stems from the facts, that sampling is not necessary in for fastseg and that a dynamic programming approach is used for calculation of the segments' first and higher order moments.

For further information regarding the algorithm and its assessment see the fastseg homepage at http://www.bioinf.jku.at/software/fastseg/fastseg.html

2 Getting started

To load the package, enter the following in your R session:

```
> library(fastseg)
```

2.1 Data

According to the DNAcopy package from bioconductor we selected a subset of the data set presented in (Snijders et al., 2001). This data set will be called coriell. The data correspond to two array CGH studies of fibroblast cell strains. [1] In particular, the studies **GM05296** and **GM13330** were chosen. After selecting only the mapped data from chromosomes 1-22 and X, there are 2271 data points.

To prepare the data for our examples we execute the following code:

```
> data(coriell)
> head(coriell)
```

```
        Clone Chromosome Position Coriell.05296 Coriell.13330
1  GS1-232B23          1        1      0.000359      0.207470
2  RP11-82d16          1      469      0.008824      0.063076
3  RP11-62m23          1     2242     -0.000890      0.123881
4  RP11-60j11          1     4505      0.075875      0.154343
5 RP11-111O05          1     5441      0.017303     -0.043890
6  RP11-51b04          1     7001     -0.006770      0.094144
```

[1] http://www.nature.com/ng/journal/v29/n3/suppinfo/ng754_S1.html

```
> samplenames <- colnames(coriell)[4:5]
> data <- as.matrix(coriell[4:5])
> #data[is.na(data)] <- median(data, na.rm=TRUE)
> chrom <- coriell$Chromosome
> maploc <- coriell$Position
```

The main functions of the package are `fastseg` and `toDNAcopyObj`. The first on runs the segmentation algorithm and the latter converts the segmentation results the a DNAcopy object which will be quite helpful for plot functions.

2.2 File formats

The package can handle different file formats: GRanges, ExpressionSet objects, matrix or a vector.

2.2.1 Vector

```
> data2 <- data[, 1]
> res <- fastseg(data2)
> head(res)
```

```
GRanges object with 6 ranges and 5 metadata columns:
      seqnames    ranges strand |          ID  num.mark    seg.mean  startRow
         <Rle> <IRanges>  <Rle> | <character> <numeric>   <numeric> <integer>
  [1]        1    1-1227      * |     sample1      1227 -0.00360432         1
  [2]        1 1228-1270      * |     sample1        43  0.46162281      1228
  [3]        1 1271-1357      * |     sample1        87  0.00431766      1271
  [4]        1 1358-1372      * |     sample1        15 -0.65108133      1358
  [5]        1 1373-2214      * |     sample1       842  0.01498080      1373
  [6]        1 2215-2271      * |     sample1        57  0.61411642      2215
        endRow
     <integer>
  [1]      1227
  [2]      1270
  [3]      1357
  [4]      1372
  [5]      2214
  [6]      2271
  -------
  seqinfo: 1 sequence from an unspecified genome; no seqlengths
```

```
>
>
```

2.2.2 Matrix

```
> data2 <- data[1:400, ]
> res <- fastseg(data2)
> head(res)
```

```
GRanges object with 6 ranges and 5 metadata columns:
      seqnames    ranges strand |            ID  num.mark    seg.mean  startRow
         <Rle> <IRanges>  <Rle> |   <character> <numeric>   <numeric> <integer>
  [1]        1      1-80      * | Coriell.05296        80  0.01681567         1
  [2]        1     81-84      * | Coriell.05296         4  0.13437475        81
  [3]        1    85-400      * | Coriell.05296       316  0.00326755        85
  [4]        1      1-91      * | Coriell.13330        91  0.01615064         1
  [5]        1    92-140      * | Coriell.13330        49  0.48524367        92
  [6]        1   141-400      * | Coriell.13330       260 -0.03233950       141
        endRow
     <integer>
  [1]       80
  [2]       84
  [3]      400
  [4]       91
  [5]      140
  [6]      400
  -------
  seqinfo: 1 sequence from an unspecified genome; no seqlengths
```

2.2.3 GRanges objects

```
> library("GenomicRanges")
> ## with both individuals
> gr <- GRanges(seqnames=chrom,
+         ranges=IRanges(maploc, end=maploc))
> mcols(gr) <- data
> colnames(mcols(gr)) <- samplenames
> res <- fastseg(gr)
> head(res)
```

```
GRanges object with 6 ranges and 5 metadata columns:
      seqnames        ranges strand |            ID  num.mark   seg.mean
         <Rle>     <IRanges>  <Rle> |   <character> <integer>  <numeric>
  [1]        1      1-240001      * | Coriell.05296       141  0.0197312
  [2]       10       1-65001      * | Coriell.05296        57 -0.0106129
  [3]       10  66906-108904      * | Coriell.05296        43  0.4516093
  [4]       10 110001-142001      * | Coriell.05296        34  0.0040314
  [5]       11       1-34421      * | Coriell.05296        52  0.0116384
  [6]       11   35417-39624      * | Coriell.05296        14 -0.6510813
```

```
       startRow    endRow
      <integer> <integer>
  [1]         1       142
  [2]         1        58
  [3]        59       102
  [4]       103       137
  [5]         1        53
  [6]        54        68
  -------
  seqinfo: 23 sequences from an unspecified genome; no seqlengths

> ## with one individual
> gr2 <- gr
> data2 <- as.matrix(data[, 1])
> colnames(data2) <- "sample1"
> mcols(gr2) <- data2
> res <- fastseg(gr2)
> head(res)

GRanges object with 6 ranges and 5 metadata columns:
      seqnames        ranges strand |          ID  num.mark   seg.mean
         <Rle>     <IRanges>  <Rle> | <character> <integer>  <numeric>
  [1]        1      1-240001      * |     sample1       141  0.0197312
  [2]       10       1-65001      * |     sample1        57 -0.0106129
  [3]       10  66906-108904      * |     sample1        43  0.4516093
  [4]       10 110001-142001      * |     sample1        34  0.0040314
  [5]       11       1-34421      * |     sample1        52  0.0116384
  [6]       11   35417-39624      * |     sample1        14 -0.6510813
       startRow    endRow
      <integer> <integer>
  [1]         1       142
  [2]         1        58
  [3]        59       102
  [4]       103       137
  [5]         1        53
  [6]        54        68
  -------
  seqinfo: 23 sequences from an unspecified genome; no seqlengths

>
```

2.2.4 ExpressionSet objects

```
> library(oligo)
> eSet <- new("ExpressionSet")
```

```
> assayData(eSet) <- list(intensity=data)
> featureData(eSet) <- new("AnnotatedDataFrame",
+         data=data.frame(
+                 chrom = paste("chr",chrom,sep=""),
+                 start = maploc,
+                 end   = maploc,stringsAsFactors=FALSE))
> phenoData(eSet) <- new("AnnotatedDataFrame",
+         data=data.frame(samples=samplenames))
> sampleNames(eSet) <- samplenames
> res <- fastseg(eSet)
> head(res)

GRanges object with 6 ranges and 5 metadata columns:
      seqnames        ranges strand |            ID  num.mark   seg.mean
         <Rle>     <IRanges>  <Rle> |   <character> <integer>  <numeric>
  [1]     chr1      1-240001      * | Coriell.05296       141  0.0197312
  [2]    chr10       1-65001      * | Coriell.05296        57 -0.0106129
  [3]    chr10  66906-108904      * | Coriell.05296        43  0.4516093
  [4]    chr10 110001-142001      * | Coriell.05296        34  0.0040314
  [5]    chr11       1-34421      * | Coriell.05296        52  0.0116384
  [6]    chr11   35417-39624      * | Coriell.05296        14 -0.6510813
       startRow    endRow
      <integer> <integer>
  [1]         1       142
  [2]         1        58
  [3]        59       102
  [4]       103       137
  [5]         1        53
  [6]        54        68
  -------
  seqinfo: 23 sequences from an unspecified genome; no seqlengths
```

2.2.5 Vector

```
> data2 <- data[, 1]
> res <- fastseg(data2)
> head(res)

GRanges object with 6 ranges and 5 metadata columns:
      seqnames    ranges strand |          ID  num.mark    seg.mean  startRow
         <Rle> <IRanges>  <Rle> | <character> <numeric>   <numeric> <integer>
  [1]        1    1-1227      * |     sample1      1227 -0.00360432         1
  [2]        1 1228-1270      * |     sample1        43  0.46162281      1228
  [3]        1 1271-1357      * |     sample1        87  0.00431766      1271
  [4]        1 1358-1372      * |     sample1        15 -0.65108133      1358
  [5]        1 1373-2214      * |     sample1       842  0.01498080      1373
```

```
  [6]        1 2215-2271      * |     sample1        57  0.61411642      2215
       endRow
    <integer>
  [1]      1227
  [2]      1270
  [3]      1357
  [4]      1372
  [5]      2214
  [6]      2271
  -------
  seqinfo: 1 sequence from an unspecified genome; no seqlengths

>
>
```

2.2.6 Matrix

```
> data2 <- data[1:400, ]
> res <- fastseg(data2)
> head(res)

GRanges object with 6 ranges and 5 metadata columns:
      seqnames    ranges strand |            ID  num.mark    seg.mean  startRow
         <Rle> <IRanges>  <Rle> |   <character> <numeric>   <numeric> <integer>
  [1]        1      1-80      * | Coriell.05296        80  0.01681567         1
  [2]        1     81-84      * | Coriell.05296         4  0.13437475        81
  [3]        1    85-400      * | Coriell.05296       316  0.00326755        85
  [4]        1      1-91      * | Coriell.13330        91  0.01615064         1
  [5]        1    92-140      * | Coriell.13330        49  0.48524367        92
  [6]        1   141-400      * | Coriell.13330       260 -0.03233950       141
       endRow
    <integer>
  [1]        80
  [2]        84
  [3]       400
  [4]        91
  [5]       140
  [6]       400
  -------
  seqinfo: 1 sequence from an unspecified genome; no seqlengths
```

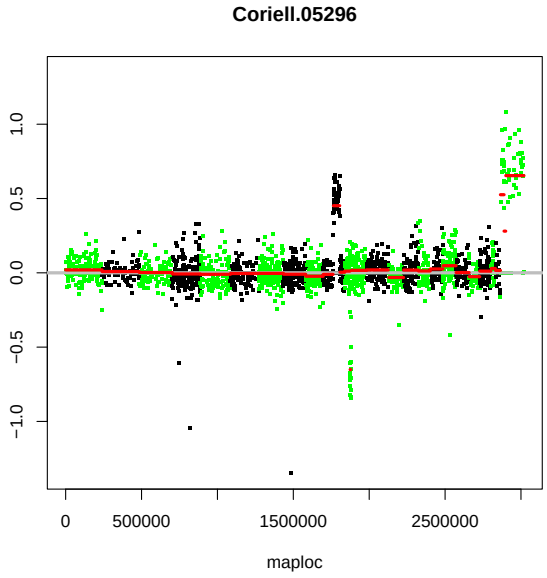
2.3 Plotting the segmentation results

For plotting the data we have to generate an `DNAcopy` object out of the segmentation results:

```
> ## with both individuals
> gr <- GRanges(seqnames=chrom,
+         ranges=IRanges(maploc, end=maploc))
> mcols(gr) <- data
> colnames(mcols(gr)) <- samplenames
> res <- fastseg(gr,segMedianT=0.2)
```

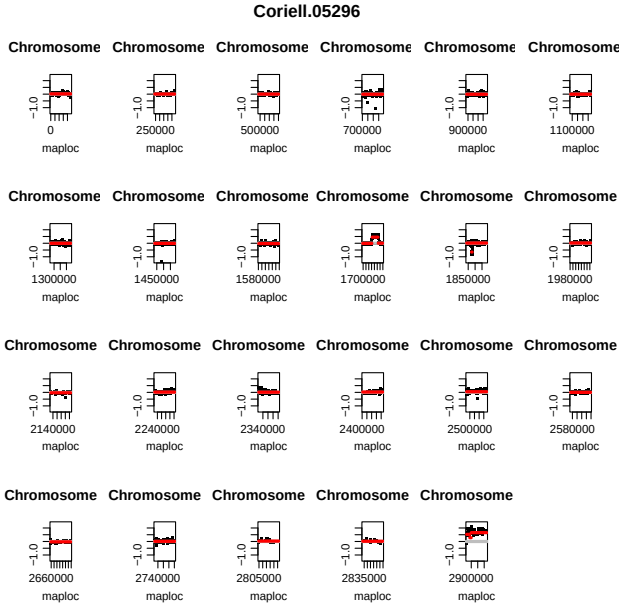
The plotting is done via the `plot` function of `DNAcopy`:

```
> segPlot(gr,res, plot.type="w")
```



Or alternatively:

```
> segPlot(gr,res, plot.type="s")
```



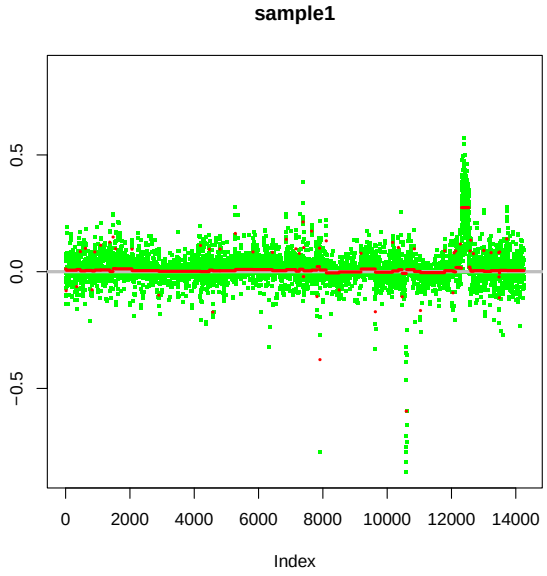
2.4 Performance of the method

Here we show that `fastseg` outperforms `DNAcopy` with respect to computational time on summarized microarray data. The quality of the segmentation result of both `fastseg` and `DNAcopy` depends strongly on the methods' parameters.
The data is a small subset of copy number calls which were produced by the `cn.farms` algorithm Clevert et al. (2011) from an Affymetrix SNP microarray experiment of a HapMap sample.

```
> data(fastsegData)
> system.time(res <- fastseg(fastsegData))
```

```
   user  system elapsed
  0.259   0.001   0.261
```

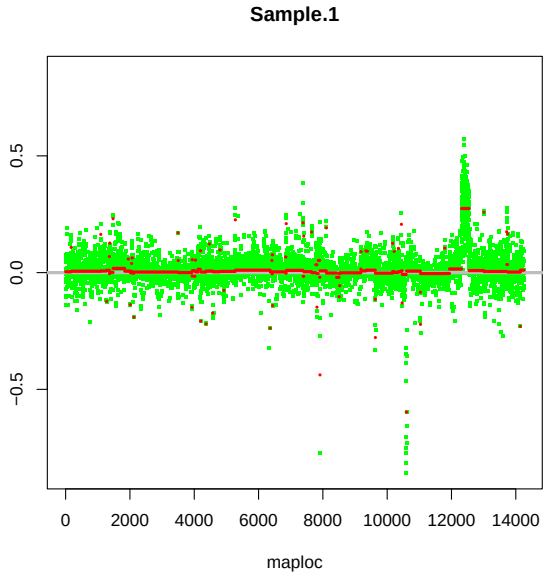
```
> segPlot(fastsegData,res, plot.type="w")
```




```
> library(DNAcopy)
> cna <- DNAcopy::CNA(fastsegData,chrom="chr1",maploc=1:length(fastsegData))
> system.time(res2 <- DNAcopy::segment(cna))

Analyzing: Sample.1
   user  system elapsed
  6.805   0.015  10.688

> plot(res2, plot.type="w", xmaploc=TRUE)
```



3 Future Extensions

We are planning to program a parallelized version of this package. Furthermore we will enhance the plot functions by our own.

4 How to cite this package

If you use this package for research that is published later, you are kindly asked to cite it as follows: (Klambauer et al., 2011).

To obtain BibTEX entries of the two references, you can enter the following into your R session:

```
> toBibtex(citation("fastseg"))
```

References

Baldi, P. and Long, A. D. (2001). A Bayesian framework for the analysis of microarray expression data: regularized t -test and statistical inferences of gene changes. *Bioinformatics*, 17(6):509–519.

Clevert, D.-A., Mitterecker, A., Mayr, A., Klambauer, G., Tuefferd, M., Bondt, A. D., Talloen, W., Göhlmann, H., and Hochreiter, S. (2011). cn.FARMS: a latent variable model to detect copy number variations in microarray data with a low false discovery rate. *Nucleic Acids Res.*, 39(12):e79.

Klambauer, G., Mitterecker, A., Clevert, D.-A., and Hochreiter, S. (2011). fastseg: a fast segmentation algorithm. *Unknown*, 99(99):99–99.

Olshen, A. B., Venkatraman, E. S., Lucito, R., and Wigler, M. (2004). Circular binary segmentation for the analysis of array-based DNA copy number data. *Biostatistics*, 5:557–72.

Snijders, A. M., Nowak, N., Segraves, R., Blackwood, S., Brown, N., Conroy, J., Hamilton, G., Hindle, A. K., Huey, B., Kimura, K., S, S. L., Myambo, K., Palmer, J., Ylstra, B., Yue, J. P., Gray, J. W., Jain, A. N., Pinkel, D., and Albertson, D. G. (2001). Assembly of microarrays for genome-wide measurement of DNA copy number. *Nat. Genet.*, 29:263–4.