

FocalCall: An R package for the annotation of focal copy number aberrations.

Oscar Krijgsman

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Department of Pathology VU University Medical Center the Netherlands
Current adres: Department of Molecular Oncology Netherlands Cancer
Institute the Netherlands

`oscarkrijgsman@gmail.com o.krijgsman@nki.nl`

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1 Overview

To identify somatic focal copy number aberrations (CNAs) in cancer specimens and distinguish them from germ-line copy number variations (CNVs) we developed a software package named, focalCall. focalCall permits user-defined size cut-offs to recognize focal aberrations and builds on established array CGH segmentation and calling algorithms. To differentiate CNAs from CNVs the algorithm can either make use of a matched normal reference signal or, if this is not available, an external CNV track. focalCall furthermore differentiates between homozygous and hemizygous deletions as well as gains and amplifications and is applicable to high-resolution array and sequencing data.

2 Example

In this section we will use `focalCall` to analyse the dataset previously published by (Bierkens et al., 2013) Bierkens et al. (2013) and preprocessed using (van de Wiel et al., 2007) by Wiel et al. (2007). The example set used here only contains complete chromosome 2. For the other chromosomes only a small portion of the CGH probes are included. The complete dataset can be downloaded from the NCBI Gene Expression Omnibus (GEO), accession number GSE34575. First, we load the required packages and the data:

```
> library(focalCall)
> data(BierkensCNA)
```

Next, we apply the `focalCall` function which:

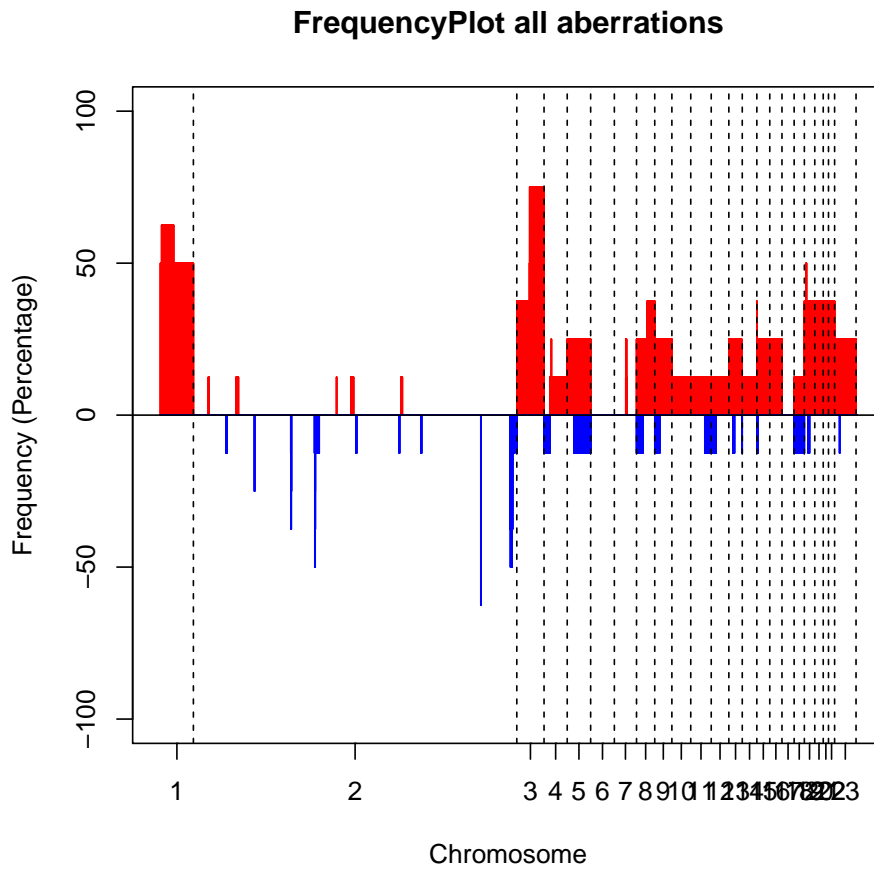
- detects all aberrations smaller than `focalSize` in Mb in the tumor data (CGHset)
- calculates peak regions for each genomic region where recurrent focal CNAs are detected
- compare each peak region to known copy number variants (CNVset)
- returns calls object with calls for focal CNA included
- report all focal CNAs as figures and tables

```
> calls_focals<-focalCall(CGHset, CNVset, focalSize = 3, minFreq=2)
```

```
Array resolution too low for calling aberrations smaller than 3MB.
Counted number of segments for each tumor sample
Generated matrix with detected aberrations < 3 Mb...
Start detection of peak regions...
Simple_ 1
Complex_ 2
Complex_ 3
Complex_ 4
Matching CNV list to copynumber data ...
Generating output files...
Written text file to workDir...
Written 'focalCall.RData' to workDir...
FINISHED!
Total time: 0 minutes
```

A frequency plot of all aberrations and all focal aberrations can be generated using `FreqPlot` and `FreqPlotfocal`.

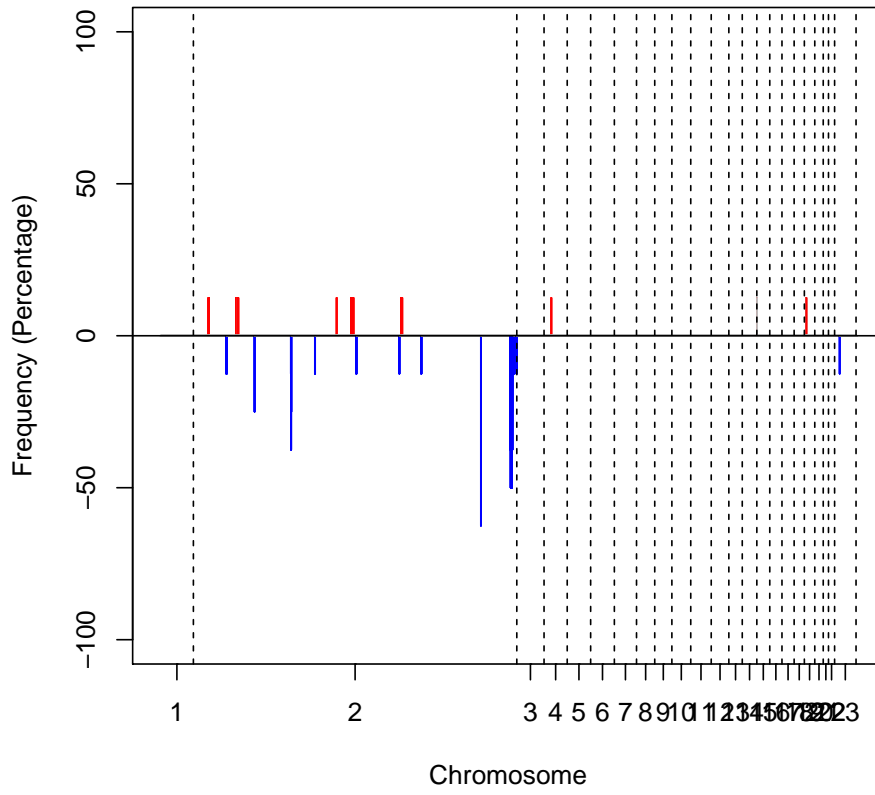
```
> FreqPlot(calls_focals, header="FrequencyPlot all aberrations")
```



```
> FreqPlotfocal(calls_focals, header="FrequencyPlot all aberrations")
```

n

FrequencyPlot all aberrations



Alternatively, we can generate files for visualisation in IGV with `igvFiles`. The files will be written to the home directory and can be loaded in IGV directly.

```
> igvFiles(calls_focals)
```

```
Generated .SEG file for loading in IGV
```

```
Generated .IGV file for loading in IGV
```

```
Generated .IGV file for loading in IGV
```

References

- Bierkens, M., Krijgsman, O., Wilting, S., Bosch, L., Jaspers, A., Meijer, G., Meijer, C., Snijders, P., Ylstra, B., and RD., S. (2013). Focal aberrations indicate *eya2* and *hsa-mir-375* as oncogene and tumor suppressor in cervical carcinogenesis. *Genes Chromosomes Cancer*, 52:56–68.
- van de Wiel, M. A., Kim, K. I., Vosse, S. J., van Wieringen, W. N., Wilting, S. M., and Ylstra, B. (2007). Calling aberrations for array CGH tumor profiles. *Bioinformatics*, 23:892–894.

3 Session Information

The version number of R and packages loaded for generating the vignette were:

```
> sessionInfo()
```

```
R version 3.6.1 (2019-07-05)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Ubuntu 18.04.3 LTS
```

```
Matrix products: default
BLAS: /home/biocbuild/bbs-3.10-bioc/R/lib/libRblas.so
LAPACK: /home/biocbuild/bbs-3.10-bioc/R/lib/libRlapack.so
```

```
locale:
```

```
[1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C
[3] LC_TIME=en_US.UTF-8      LC_COLLATE=C
[5] LC_MONETARY=en_US.UTF-8  LC_MESSAGES=en_US.UTF-8
[7] LC_PAPER=en_US.UTF-8    LC_NAME=C
[9] LC_ADDRESS=C             LC_TELEPHONE=C
[11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C
```

```
attached base packages:
```

```
[1] parallel stats graphics grDevices utils datasets methods
[8] base
```

```
other attached packages:
```

```
[1] focalCall_1.20.0 CGHcall_2.48.0 snowfall_1.84-6.1
[4] snow_0.4-3 CGHbase_1.46.0 marray_1.64.0
[7] limma_3.42.0 Biobase_2.46.0 BiocGenerics_0.32.0
[10] DNACopy_1.60.0 impute_1.60.0
```

```
loaded via a namespace (and not attached):
```

```
[1] compiler_3.6.1 tools_3.6.1
```