CGHcall: Calling aberrations for array CGH tumor profiles.

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Contents

1 Overview

CGHcall allows users to make an objective and effective classification of their aCGH data into copy number states (loss, normal, gain or amplification). This document provides an overview on the usage of the CGHcall package. For more detailed information on the algorithm and assumptions we refer to the article (van de Wiel et al., 2007) and its supplementary material. As example data we attached the first five samples of the Wilting dataset (Wilting et al., 2006). After filtering and selecting only the autosomes 4709 datapoints remained.

2 Example

In this section we will use CGHcall to call and visualize the aberrations in the dataset described above. First, we load the package and the data:

```
> library(CGHcall)
> data(WiltingData)
> Wilting <- cghRaw(WiltingData)
```

Next, we apply the `preprocess` function which:

- removes data with unknown or invalid position information.
- shrinks the data to `nchrom` chromosomes.
- removes data with more than `maxmiss` % missing values.
- imputes missing values using `impute.knn` from the package `impute` (Troyanskaya et al., 2001).

```
> cghdata <- preprocess(Wilting, maxmiss=30, nchrom=22)
```

```
Changing impute.knn parameter k from 10 to 4 due to small sample size.
```

To be able to compare profiles they need to be normalized. In this package we provide very basic global median or mode normalization. Of course, other methods can be used outside this package. This function also contains smoothing of outliers as implemented in the DNAcopy package (Venkatraman and Olshen, 2007). Furthermore, when the proportion of tumor cells is not 100% the ratios can be corrected. See the article and the supplementary material for more information on cellularity correction (van de Wiel et al., 2007).

```
> tumor.prop <- c(0.75, 0.9, 0.8, 1, 1)
> norm.cghdata <- normalize(cghdata, method="median", cellularity=tumor.prop, smoothO
```

```
Applying median normalization ...
Smoothing outliers ...
Adjusting for cellularity ...
Cellularity sample 1 :  0.75
Cellularity sample 2 :  0.9
Cellularity sample 3 :  0.8
Cellularity sample 4 :  1
Cellularity sample 5 :  1
```

The next step is segmentation of the data. This package only provides a simple wrapper function that applies the `DNAcopy` algorithm (Venkatraman and Olshen, 2007). Again, other segmentation algorithms may be used. To save time we will limit our analysis to the first two samples from here on.

```
> norm.cghdata <- norm.cghdata[,1:2]
> seg.cghdata <- segmentData(norm.cghdata, method="DNAcopy")

Start data segmentation ..
Analyzing: Sample.1
Analyzing: Sample.2
```

Post-segmentation normalization allows to better set the zero level after segmentation

```
> postseg.cghdata <- postsegnormalize(seg.cghdata)
```

Now that the data have been normalized and segments have been defined, we need to determine which segments should be classified as losses, normal, gains or amplifications.

```
> result <- CGHcall(postseg.cghdata)

[1] "changed"
EM algorithm started ...
[1] "Total number of segments present in the data: 113"
[1] "Number of segments used for fitting the model: 113"
         used (Mb) gc trigger (Mb) max used (Mb)
Ncells 542101 29.0     899071 48.1   899071 48.1
Vcells 943621  7.2    1598044 12.2  1598025 12.2
Calling iteration 1 :
     j        rl       mudl        musl        mun       mug      mudg      mua
[1,] 2 -3770.814 -0.8429234 -0.2959666 0.01151765 0.3355313 0.5735946 1.073453
           sddl       sdsl         sdn       sdg      sddg       sda
[1,] 0.08667158 0.08609276 0.08947486 0.1710695 0.1713615 0.1713616
         used (Mb) gc trigger (Mb) max used (Mb)
Ncells 542552 29.0     899071 48.1   899071 48.1
Vcells 944677  7.3    1598044 12.2  1598025 12.2
Calling iteration 2 :
     j        rl      mudl       musl         mun       mug      mudg      mua
[1,] 2 -3769.749 -0.848933 -0.294113 0.01683709 0.3371155 0.5763027 1.076157
           sddl       sdsl         sdn      sdg      sddg       sda
[1,] 0.08073707 0.08011538 0.08195825 0.170614 0.1709068 0.1709068
Computing posterior probabilities for all segments ...
Total time: 1 minutes
```

In CGHcall version >=2.9.0 the result of CGHcall needs to be converted to a call object. This can be a large object for large arrays.

```
> result <- ExpandCGHcall(result,postseg.cghdata)
```

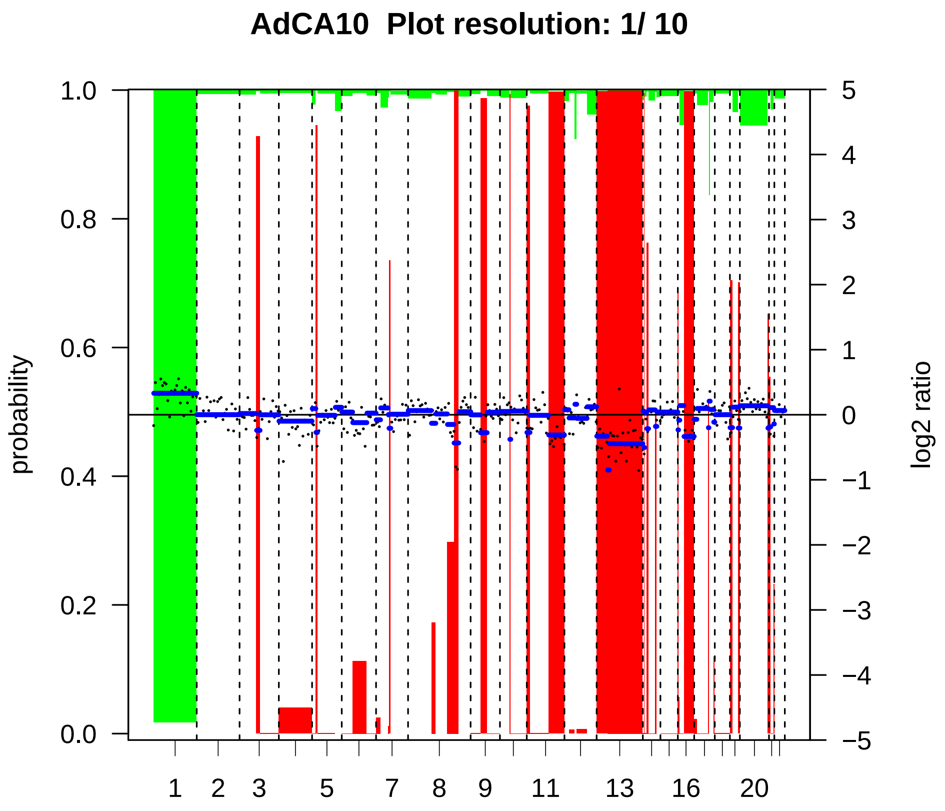
```
[1] 1
         used (Mb) gc trigger (Mb) max used (Mb)
Ncells 543886 29.1     899071 48.1   899071 48.1
Vcells 976668  7.5    1757946 13.5  1598025 12.2
         used (Mb) gc trigger (Mb) max used (Mb)
Ncells 543896 29.1     899071 48.1   899071 48.1
Vcells 990877  7.6    1757946 13.5  1748260 13.4
         used (Mb) gc trigger (Mb) max used (Mb)
Ncells 543895 29.1     899071 48.1   899071 48.1
Vcells 990876  7.6    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543913 29.1     899071 48.1   899071 48.1
Vcells 1012190  7.8    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543951 29.1     899071 48.1   899071 48.1
Vcells 1015764  7.8    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543959 29.1     899071 48.1   899071 48.1
Vcells 1019320  7.8    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543967 29.1     899071 48.1   899071 48.1
Vcells 1022876  7.9    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543975 29.1     899071 48.1   899071 48.1
Vcells 1026432  7.9    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  543979 29.1     899071 48.1   899071 48.1
Vcells 1029987  7.9    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544006 29.1     899071 48.1   899071 48.1
Vcells 1051340  8.1    1757946 13.5  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544763 29.1     899071 48.1   899071 48.1
Vcells 1060635  8.1    1757946 13.5  1748260 13.4
[1] 2
```

```
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544767 29.1     899071 48.1   899071 48.1
Vcells 1074844  8.3    1925843 14.7  1748260 13.4
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544768 29.1     899071 48.1   899071 48.1
Vcells 1074845  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544767 29.1     899071 48.1   899071 48.1
Vcells 1074844  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544771 29.1     899071 48.1   899071 48.1
Vcells 1078397  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544767 29.1     899071 48.1   899071 48.1
Vcells 1074844  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544775 29.1     899071 48.1   899071 48.1
Vcells 1078400  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544783 29.1     899071 48.1   899071 48.1
Vcells 1081956  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544791 29.1     899071 48.1   899071 48.1
Vcells 1085512  8.3    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544795 29.1     899071 48.1   899071 48.1
Vcells 1089067  8.4    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  544822 29.1     899071 48.1   899071 48.1
Vcells 1110420  8.5    1925843 14.7  1760801 13.5
          used (Mb) gc trigger (Mb) max used (Mb)
Ncells  549010 29.4     899071 48.1   899071 48.1
Vcells 1092509  8.4    1925843 14.7  1925490 14.7
FINISHED!
Total time: 0 minutes
```

To visualize the results per profile we use the `plotProfile` function:

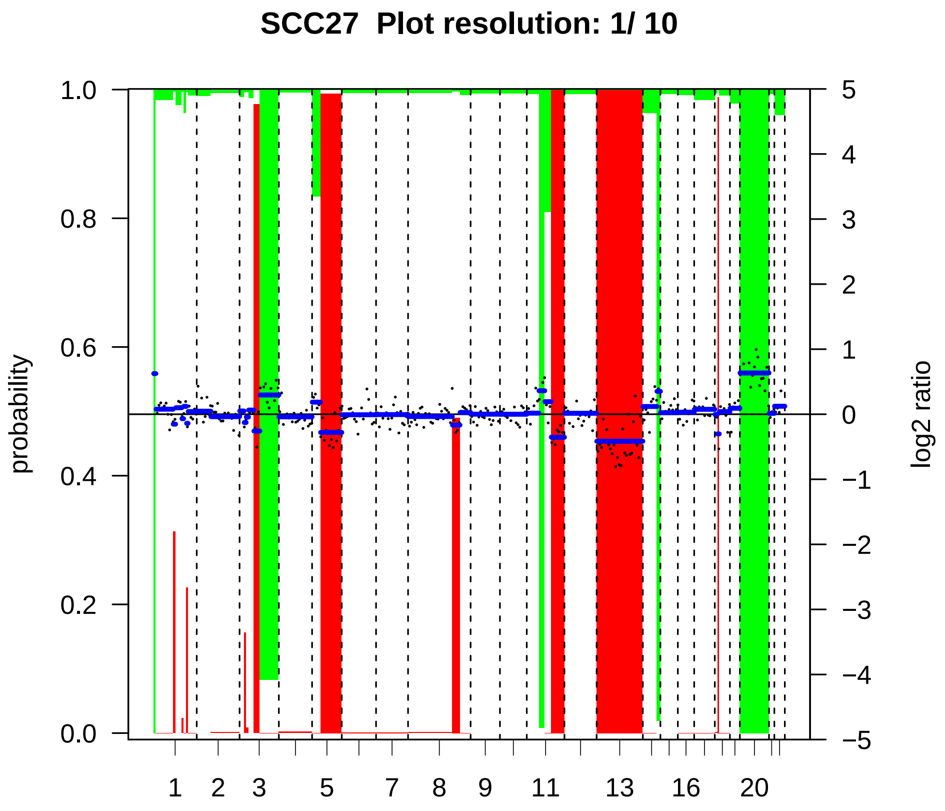
```
> plot(result[,1])
```

```
Plotting sample AdCA10
```



```
> plot(result[,2])
```

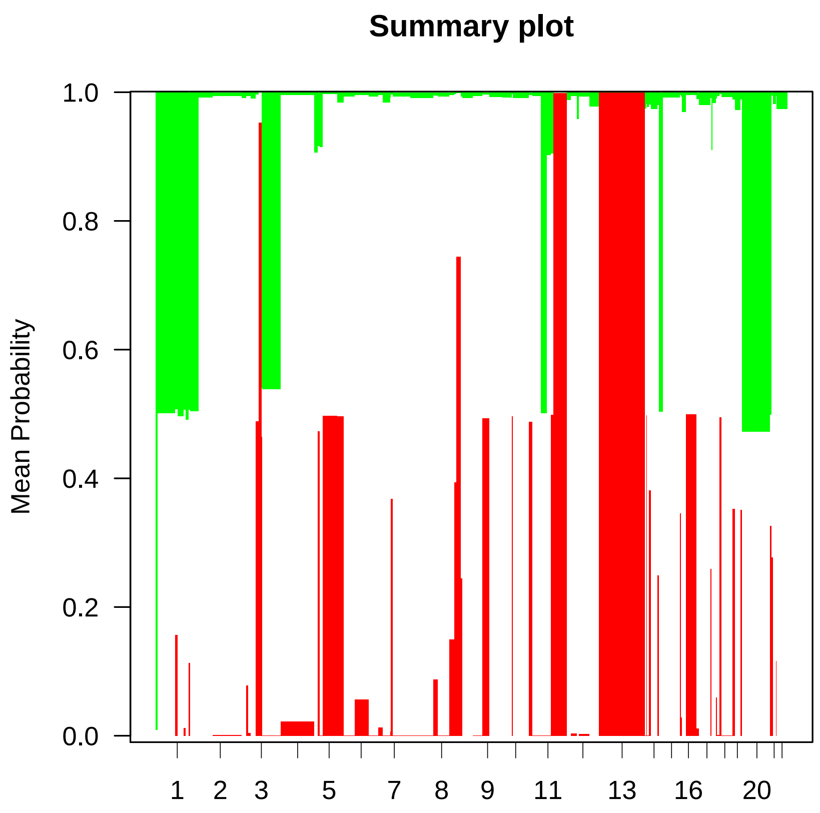
```
Plotting sample SCC27
```



Alternatively, we can create a summary plot of all the samples:

```
> summaryPlot(result)
```

```
Adding sample AdCA10 to summary plot.
Adding sample SCC27 to summary plot.
```



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