Bioconductor's aCGH package

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Contents

1 Overview

This document presents an overview of the `aCGH` package, which provides wide basic functions for reading, analyzing and plotting array Comparative Genomic Hybridization data (Snijders et al. (2001)). Specific example for reading data in is using output of the custom freely available programs, SPOT and SPROC (Jain et al. (2002)). These programs provide image quantification and pre-processing. Outputs of all the other image processing software need to be combined into a single file containing observed values for each clone and samples and then read in as a matrix.

2 Data

The data used in the example was generated in in lab of Dr. Fred Waldman at UCSF Comprehensive Cancer Center (Nakao et al. (2004)).Array CGH has been done on 125 colorectal fresh-frozen primary tumors and the associations with various phenotypes were analyzed. To reduce running time, only 40 samples are used in the examples.

3 Examples

3.1 Creating aCGH object from log2.ratios and clone info files

Each array CGH object has to contain the log2ratios representing relative copy number along with the mapping information including but not limited to clone name, chromosome and kb relative to the chromosome. Optionally there may be phenotypes associated with each sample.

```
> library(aCGH)
> datadir <- system.file(package = "aCGH")
> datadir <- paste(datadir, "/examples", sep="")
> clones.info <-
+       read.table(file = file.path(datadir, "clones.info.ex.txt"),
+                  header = T, sep = "\t", quote="", comment.char="")
> log2.ratios <-
+       read.table(file = file.path(datadir, "log2.ratios.ex.txt"),
+                  header = T, sep = "\t", quote="", comment.char="")
> pheno.type <-
+       read.table(file = file.path(datadir, "pheno.type.ex.txt"),
+                  header = T, sep = "\t", quote="", comment.char="")
> ex.acgh <- create.aCGH(log2.ratios, clones.info, pheno.type)
```

Note that when working with your own data, you will need to specify absolute path to those files ot the path relative to your working folder. For instance, if you are working in the folder *Project1* your data files are placed in the subfolder *Project1/Data*, then *datadir = "Data"* if you are using relative path.

3.2 Filtering and imputation for objects of class aCGH

Here we remove unmapped clones and clones mapping to Y chromosome, screen out clones missing in more than 25

```
> ex.acgh <-
+     aCGH.process(ex.acgh, chrom.remove.threshold = 23, prop.missing = .25, sample.quality.t
```

Here we impute missing observations using lowess approach. Note that occasionally, majority of the observations on chromosome Y may be missing causing imputing function to fail. Therefore, by default, the largest chromosome to be imputed is indexed as maxChrom=23 (X). Here we specify imputation for all chromosomes ; however, in this example there are no data on chromosome Y.

```
> log2.ratios.imputed(ex.acgh) <- impute.lowess(ex.acgh, maxChrom=24)

Processing chromosome  1
Processing chromosome  2
Processing chromosome  3
Processing chromosome  4
Processing chromosome  5
Processing chromosome  6
Processing chromosome  7
Processing chromosome  8
Processing chromosome  9
Processing chromosome  10
Processing chromosome  11
Processing chromosome  12
Processing chromosome  13
Processing chromosome  14
Processing chromosome  15
Processing chromosome  16
Processing chromosome  17
Processing chromosome  18
Processing chromosome  19
Processing chromosome  20
Processing chromosome  21
Processing chromosome  22
Processing chromosome  23
```

3.3 Printing, summary and basic plotting (fig. 1) for objects of class aCGH

```
> data(colorectal)
> colorectal

aCGH object
Call: aCGH.read.Sprocs(sproclist[1:40], "human.clones.info.Jul03.csv",
    chrom.remove.threshold = 23)

Number of Arrays 40
Number of Clones 2031

> summary(colorectal)

aCGH object
Call: aCGH.read.Sprocs(sproclist[1:40], "human.clones.info.Jul03.csv",
    chrom.remove.threshold = 23)

Number of Arrays 40
Number of Clones 2031
Imputed data exist
HMM states assigned
```

```
samples standard deviations are computed
genomic events are assigned
phenotype exists
```

```
> plot(colorectal)
```

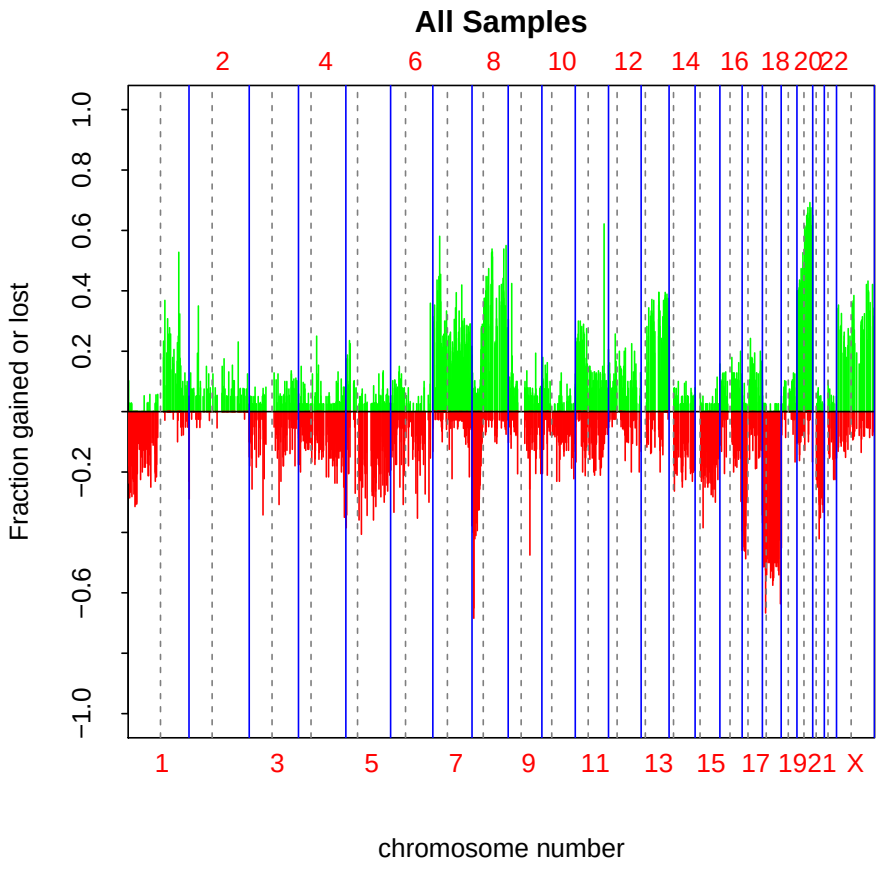

Figure 1: Basic Frequency Plot

```
> sample.names(colorectal)

 [1] "sprocCR31.txt"  "sprocCR40.txt"  "sprocCR43.txt"  "sprocCR59.txt"
 [5] "sprocCR63.txt"  "sprocCR73.txt"  "sprocCR75.txt"  "sprocCR77.txt"
 [9] "sprocCR96.txt"  "sprocCR98.txt"  "sprocCR100.txt" "sprocCR106.txt"
[13] "sprocCR112.txt" "sprocCR122.txt" "sprocCR124.txt" "sprocCR131.txt"
[17] "sprocCR135.txt" "sprocCR137.txt" "sprocCR146.txt" "sprocCR148.txt"
[21] "sprocCR150.txt" "sprocCR154.txt" "sprocCR159.txt" "sprocCR163.txt"
[25] "sprocCR169.txt" "sprocCR178.txt" "sprocCR180.txt" "sprocCR186.txt"
[29] "sprocCR193.txt" "sprocCR200.txt" "sprocCR204.txt" "sprocCR210.txt"
[33] "sprocCR212.txt" "sprocCR217.txt" "sprocCR219.txt" "sprocCR227.txt"
[37] "sprocCR232.txt" "sprocCR244.txt" "sprocCR246.txt" "sprocCR248.txt"

> phenotype(colorectal)[1:4,]

  id age sex stage loc           hist diff gstm1 gstt1 nqo K12 K13 MTHFR ERCC1
1 31  70   0     1   0 Adenocarcinoma    1     0     1   1   1   2     2     1
2 40  71   0     1   1 Adenocarcinoma    1     1     1   1   2   2     2     2
3 43  59   1     1   0 Adenocarcinoma   NA     1     1   1   2   2     2     1
4 59  72   0     2   1 Adenocarcinoma    1     1     1   1   2   2     1    NA
  bat26 bat25 D5S346 D17S250 D2S123                          mi2      LOH k12
1     0     0      0       0      0           0/1 unstable loci negative   1
2     0     0      1       1      1 >2 loci unstable, (NCI def) negative   0
3     0     0      0       0      0           0/1 unstable loci negative   0
4     0     0      0       0      0           0/1 unstable loci negative   0
  K12AA k13 K13AA M677 M1298 p16 p14 mlh1 BAT26 mlh1c                mi misum
1   GTT   0     .    1     0   1   0    1     0     0 0/1 unstable loci     0
2     .   0     .    1     0   0   0    0     0     0  >2 loci unstable     3
3     .   0     .    1     0   2   0    0     0     0 0/1 unstable loci     0
4     .   0     .    0     1   0   1    0     0     0 0/1 unstable loci     0
   CGHSTAT
1 Complete
2 Complete
3 Complete
4 Not Done
```

3.4 Reading Sproc files

Here we demonstrate reading of the sproc files and combining them into one array CGH object. Sproc file format is specific to the custom SPROC processing software at UCSF Cancer Center.

```
> datadir <- system.file("examples", package = "aCGH")
> latest.mapping.file <-
+         file.path(datadir, "human.clones.info.Jul03.txt")
> ex.acgh <-
+         aCGH.read.Sprocs(dir(path = datadir,pattern = "sproc",
+                         full.names = TRUE), latest.mapping.file,
+                         chrom.remove.threshold = 23)
```

```
Trying to read  /tmp/Rtmp3AMn6Y/Rinst7772fdaa/aCGH/examples/sprocCR40.txt
Trying to read  /tmp/Rtmp3AMn6Y/Rinst7772fdaa/aCGH/examples/sprocCR43.txt

Averaging duplicated clones
CTB-102E19          692 693
CTB-112F7          1692 1693
CTB-142O24          1640 1641
CTB-339E12          1633 1634
CTB-36F16          1220 1221
DMPC-HFF#1-61H8          1662 1663
GS1-202O8          662 663
RP1-97B16          256 257
RP11-119J20          409 410
RP11-13C20          153 154
RP11-149G12          815 816
RP11-172D2          825 826
RP11-175H20          821 822
RP11-176L22          183 184
RP11-188C10          817 818
RP11-1L22          147 148
RP11-204M16          785 786
RP11-238H10          850 851
RP11-23G2          176 177
RP11-247E23          178 179
RP11-268N2          813 814
RP11-30M1          166 167
RP11-39A8          158 159
RP11-47E6          170 171
RP11-72C6          1006 1007
RP11-83O14          819 820
RP11-94M13          873 874

> ex.acgh

aCGH object
Call: aCGH.read.Sprocs(dir(path = datadir, pattern = "sproc", full.names = TRUE),
    latest.mapping.file, chrom.remove.threshold = 23)

Number of Arrays 2
Number of Clones 1952
```

3.5 Basic plot for batch of aCGH Sproc files. (fig. 2)

```
> plot(ex.acgh)
```

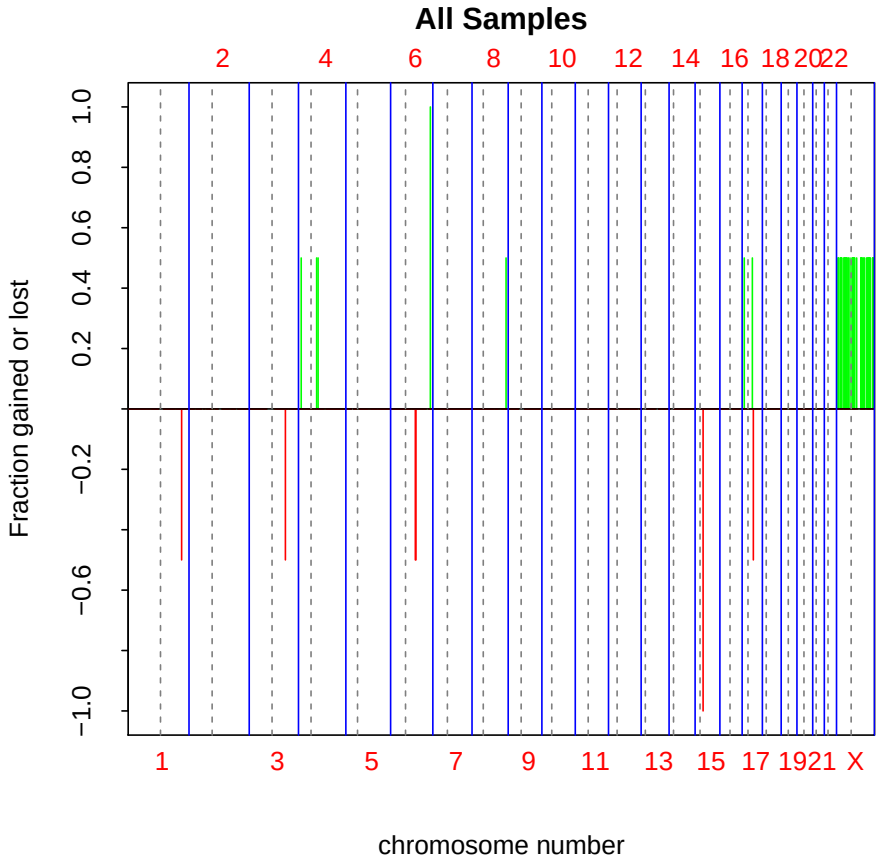

Figure 2: Basic plot for batch of aCGH Sproc files

3.6 Subsetting example

```
> cr <- colorectal[ ,1:3]
```

3.7 Basic plot for the ordered log2 ratios along the genome

The relative copy number is plotted along the genome with clones placed in the genomic order. We are plotting sample 2 here. (fig. 3). Chromosome Y is explicitely excluded.

```
> plotGenome(ex.acgh, samples=2, Y = FALSE)
```

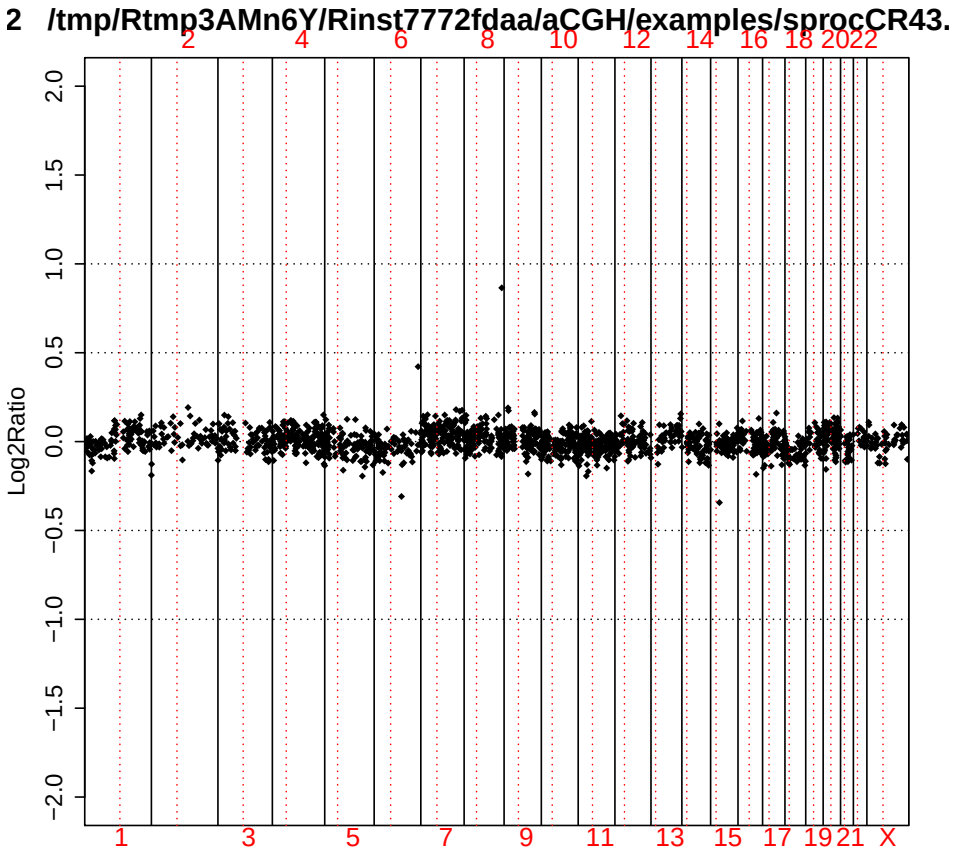

Figure 3: Basic plot for the ordered log2 ratios along the genome

3.8 Computing and plotting hmm states

Unsupervised hidden markov model is repeatedly fitted to each chromosome for varying number of states (2 , ..., 5). The number of states is determined after all fits are done usingmodel selection criterion such as AIC, BIC or delta-BIC. The model with minimal penalized negative log-likelihood is chosen for each selection criterion. Note, that some of the model fits are going to fail and are not going to be used in the final selection. Meanwhile , error message warning of the model fit failing will be printed during hmm runs. The user shoulld ignore those particular messages and related warnings.
For a given sample, each chromosome is plotted on a separate page along with its smoothed values(fig. 4). The genomic events such as transitions, focal aberrations and amplifications are indicated. The outliers are also marked.

```
> ## Determining hmm states of the clones. In the interest of time,
> ##we have commented this step out and used pre-computed results.
>
> ##hmm(ex.acgh) <- find.hmm.states(ex.acgh)
> hmm(ex.acgh) <- ex.acgh.hmm
> ## Merging hmm states
>
> hmm.merged(ex.acgh) <-
+    mergeHmmStates(ex.acgh, model.use = 1, minDiff = .25)
> ## Calculating the standard deviations for each array. Standard error is
> ##calculated for each region and then averaged across regions. The final
> ##SDs for each samples are contained in sd.samples(exa.acgh)$madGenome.
>
> sd.samples(ex.acgh) <- computeSD.Samples(ex.acgh)
> ## Finding the genomic events associated with each sample using
> ##results of the partitioning into the states.
>
> genomic.events(ex.acgh) <- find.genomic.events(ex.acgh)

Finding outliers
Finding focal low level aberrations
Finding transitions
Finding focal amplifications
Processing chromosome  1
Processing chromosome  2
Processing chromosome  3
Processing chromosome  4
Processing chromosome  5
Processing chromosome  6
Processing chromosome  7
Processing chromosome  8
Processing chromosome  9
Processing chromosome  10
Processing chromosome  11
Processing chromosome  12
```

```
Processing chromosome  13
Processing chromosome  14
Processing chromosome  15
Processing chromosome  16
Processing chromosome  17
Processing chromosome  18
Processing chromosome  19
Processing chromosome  20
Processing chromosome  21
Processing chromosome  22
Processing chromosome  23

>
> ## Plotting and printing the hmm states either to the screen or into the
> ##postscript file. Each chromosome for each sample is plotted on a separate
> ##page
>
> ##postscript("hmm.states.temp.ps");plotHmmStates(ex.acgh, sample.ind=1);dev.off()
```

```
> plotHmmStates(colorectal, sample.ind = 1, chr = 1)
```

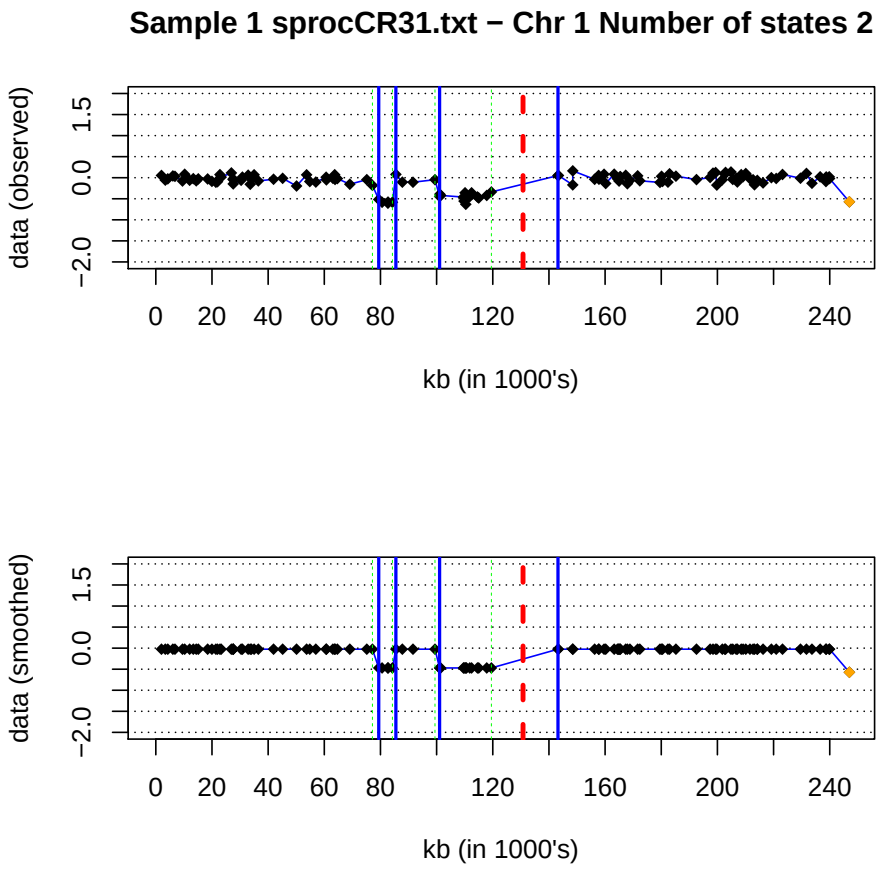

Figure 4: Plotting the hmm states found for colorectal data set.

3.9 Plotting summary of the tumor profiles

Here the distribution of various genomic events as well as their frequency by location is displayed. Run the function plotSummaryProfile(colorectal) which produces multi-page figure. Necessary to write out as ps or pdf files.

3.10 Overall frequency plot (fig. 5)

```
> plotFreqStat(colorectal, all = T)
```

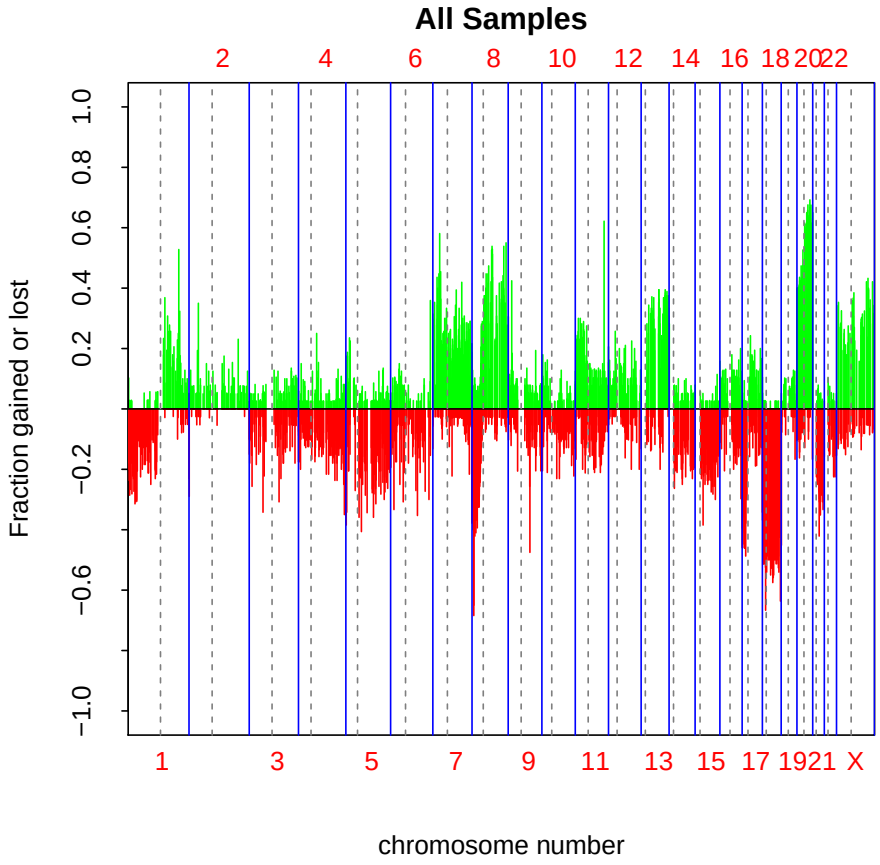

Figure 5: Overall frequency plot of the tumor profiles

summarize.clones() function is the text equivalent of plotFreqStat() - it summarizes the frequencies of changes for each clone across tumors and includes results of statistical comparisons for each clone when available.

```
> summarize.clones(colorectal)[1:10 ,]
```

	Clone	Target	Chrom	kb	NumPresent.All	NumGain.All
2	RP11-82D16	HumArray2H11_C9	1	2009	39	4
3	RP11-62M23	HumArray2H10_N30	1	3368	35	1
4	RP11-111O5	HumArray2H10_B18	1	4262	38	1
5	RP11-51B4	HumArray2H10_Q30	1	6069	35	0
6	RP11-60J11	HumArray2H10_T30	1	6817	36	1
7	RP11-813J5	HumArray2H10_B19	1	9498	30	0
8	RP11-199O1	HumArray2H10_W30	1	10284	39	1
9	RP11-188F7	HumArray2H9_C14	1	12042	36	1

```
10 RP11-178M15  HumArray2H9_F14     1 13349             35           1
11  RP11-219F4  HumArray2H9_I14     1 14391             39           1
   NumLost.All PropPresent.All PropGain.All PropLost.All
2            7            0.98         0.10         0.18
3            7            0.88         0.03         0.20
4            9            0.95         0.03         0.24
5           10            0.88         0.00         0.29
6            7            0.90         0.03         0.19
7            8            0.75         0.00         0.27
8            5            0.98         0.03         0.13
9            4            0.90         0.03         0.11
10           4            0.88         0.03         0.11
11           7            0.98         0.03         0.18
```

threshold.func() function gives the clone by sample matrix of gains and losses. "1" indicates gain and "-1" indicates loss.

```
> factor <- 3
> tbl <- threshold.func(log2.ratios(colorectal),
+             posThres=factor*(sd.samples(colorectal)$madGenome))
> rownames(tbl) <- clone.names(colorectal)
> colnames(tbl) <- sample.names(colorectal)
> tbl[1:5,1:5]
```

```
           sprocCR31.txt sprocCR40.txt sprocCR43.txt sprocCR59.txt
RP11-82D16             0             0             0            -1
RP11-62M23             0             0             0            -1
RP11-111O5             0             0             0            -1
RP11-51B4              0            NA             0            -1
RP11-60J11             0             0             0            -1
           sprocCR63.txt
RP11-82D16             1
RP11-62M23             0
RP11-111O5             1
RP11-51B4              0
RP11-60J11             0
```

fga.func() function gives the fraction of genome altered for each sample.

```
> col.fga <- fga.func(colorectal, factor=3,chrominfo=human.chrom.info.Jul03)
> cbind(gainP=col.fga$gainP,lossP=col.fga$lossP)[1:5,]
```

```
           gainP       lossP
[1,] 0.220098155 0.184029096
[2,] 0.025559893 0.004990002
[3,] 0.006184865 0.002350805
[4,] 0.107402285 0.148058176
[5,] 0.143115647 0.137430523
```

3.11 Testing association of clones with categorical, censored or continuous outcomes.

Use mt.maxT function from multtest package to test differences in group means for each clone grouped by sex. Plot the result along the genome displaying the frequencies of gains and losses as well well as height of the statistic correponsding to each clone(figs. 6 and 7.). The p-value can be adjusted and the horizontal lines indicate chosen level of significance.

```
> colnames(phenotype(colorectal))

 [1] "id"      "age"     "sex"     "stage"   "loc"     "hist"    "diff"
 [8] "gstm1"   "gstt1"   "nqo"     "K12"     "K13"     "MTHFR"   "ERCC1"
[15] "bat26"   "bat25"   "D5S346"  "D17S250" "D2S123"  "mi2"     "LOH"
[22] "k12"     "K12AA"   "k13"     "K13AA"   "M677"    "M1298"   "p16"
[29] "p14"     "mlh1"    "BAT26"   "mlh1c"   "mi"      "misum"   "CGHSTAT"

> sex <- phenotype(colorectal)$sex
> sex.na <- !is.na(sex)
> index.clones.use <- which(clones.info(colorectal)$Chrom < 23)
> colorectal.na <- colorectal[ index.clones.use,sex.na , keep=TRUE]
> dat <- log2.ratios.imputed(colorectal.na)
> resT.sex <- mt.maxT(dat, sex[sex.na], test = "t.equalvar", B = 1000)

b=10        b=20        b=30        b=40        b=50        b=60        b=70        b=80
b=110        b=120        b=130        b=140        b=150        b=160        b=170        b=
b=210        b=220        b=230        b=240        b=250        b=260        b=270        b=
b=310        b=320        b=330        b=340        b=350        b=360        b=370        b=
b=410        b=420        b=430        b=440        b=450        b=460        b=470        b=
b=510        b=520        b=530        b=540        b=550        b=560        b=570        b=
b=610        b=620        b=630        b=640        b=650        b=660        b=670        b=
b=710        b=720        b=730        b=740        b=750        b=760        b=770        b=
b=810        b=820        b=830        b=840        b=850        b=860        b=870        b=
b=910        b=920        b=930        b=940        b=950        b=960        b=970        b=
```

```
> plotFreqStat(colorectal.na, resT.sex, sex[sex.na], factor=3, titles =
+                c("Female", "Male"), X = FALSE, Y = FALSE)
```

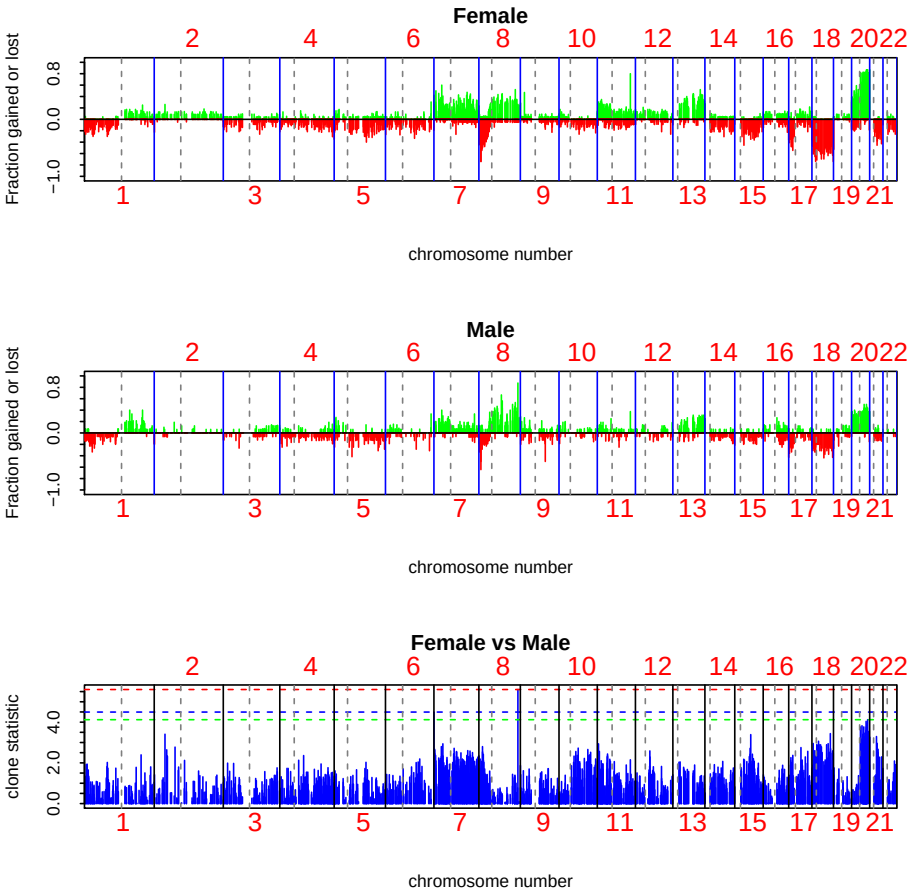

Figure 6: Frequency plots of the samples with respect to the sex groups

```
> plotSummaryProfile(colorectal, response = sex,
+                    titles = c("Female", "Male"),
+                    X = FALSE, Y = FALSE, maxChrom = 22)
```

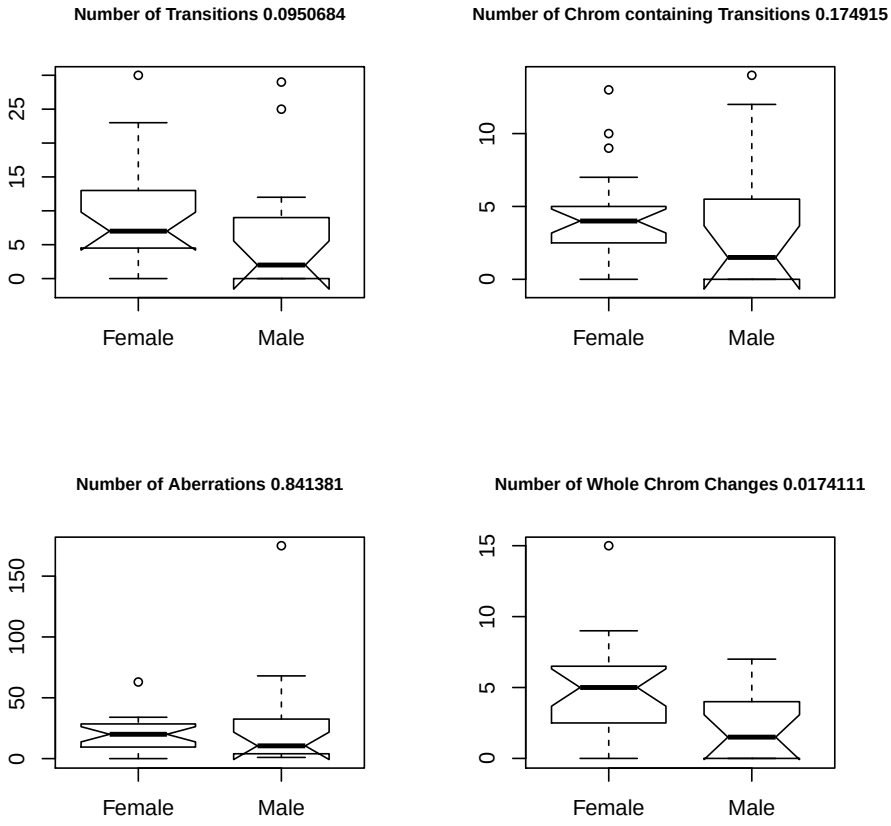

Figure 7: Plotting summary of the tumor profiles

Testing association of clones with categorical outcome for autosomal clones that are gained or lost in at least 10% of the samples. Note that the same dataset should be provided for creating *resT* object and for plotting. Pay attention that HMM-related objects including sample variability do not get subsetted at the moment. Note that currently two-stage subsetting does not work for HMM slots, i.e. two conditions (change and autosomal) need to be done in one iteration.

```
> factor <- 3
> minChanged <- 0.1
> gainloss <- gainLoss(log2.ratios(colorectal)[,sex.na], cols=1:length(which(sex.na)), thres=
> ind.clones.use <- which(gainloss$gainP >= minChanged | gainloss$lossP>= minChanged & clones
> colorectal.na <- colorectal[ind.clones.use,sex.na, keep=TRUE]
> dat <- log2.ratios.imputed(colorectal.na)
> resT.sex <- mt.maxT(dat, sex[sex.na],test = "t.equalvar", B = 1000)

b=10        b=20        b=30        b=40        b=50        b=60        b=70        b=80
b=110        b=120        b=130        b=140        b=150        b=160        b=170        b=
b=210        b=220        b=230        b=240        b=250        b=260        b=270        b=
b=310        b=320        b=330        b=340        b=350        b=360        b=370        b=
b=410        b=420        b=430        b=440        b=450        b=460        b=470        b=
b=510        b=520        b=530        b=540        b=550        b=560        b=570        b=
b=610        b=620        b=630        b=640        b=650        b=660        b=670        b=
b=710        b=720        b=730        b=740        b=750        b=760        b=770        b=
b=810        b=820        b=830        b=840        b=850        b=860        b=870        b=
b=910        b=920        b=930        b=940        b=950        b=960        b=970        b=

>
```

```
> plotFreqStat(colorectal.na, resT.sex, sex[sex.na],factor=factor,titles = c("Male", "Female"
```

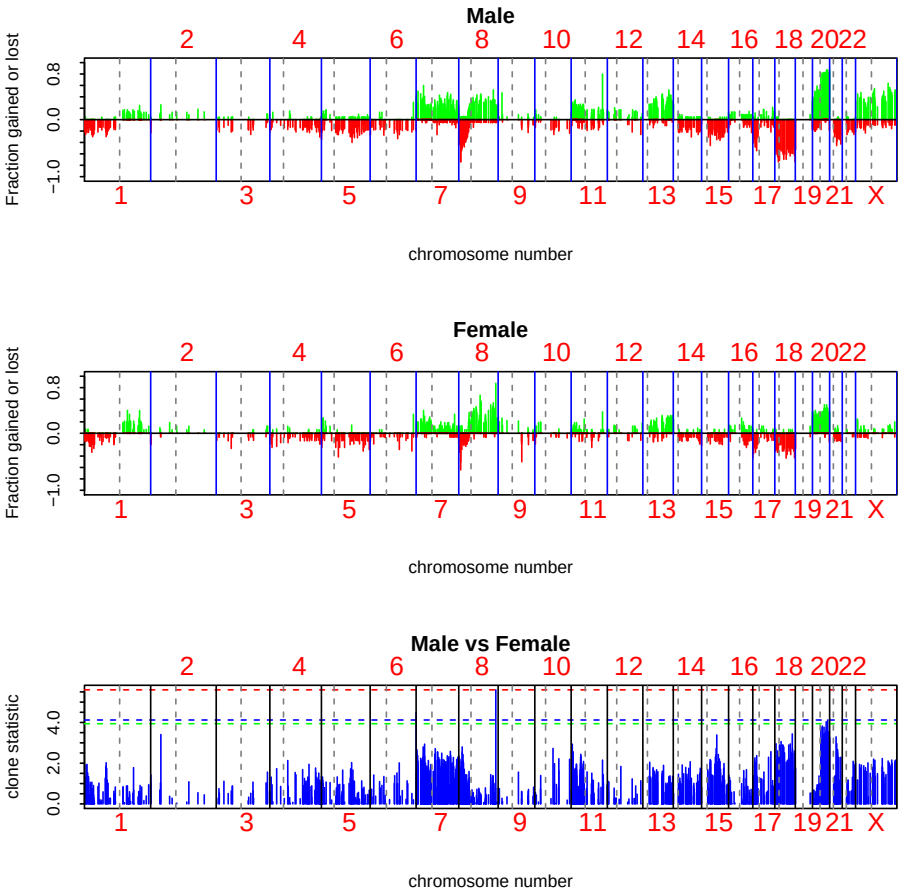

Figure 8: Frequency plots of the samples with respect to the sex groups for clones gained or lost in at least 10% of the samples

Testing association of clones with censored outcomes.Since there was no survival data available, we simulate data for a simple example to demonstrate creation and usage of basic survival object. We create an object equivalent to resT object that was created earlier. In the figure the samples are seprated into dead and alive/censored groups for ease of visualization. Nevertheless, statistic is computed and assessed for significance using proper survival object.

```
> time <- rexp(ncol(colorectal), rate = 1 / 12)
> events <- rbinom(ncol(colorectal), size = 1, prob = .5)
> surv.obj <- Surv(time,         events)
> surv.obj

 [1]   2.00874674   18.39349235+   3.56304108   22.00046050   13.66879421
 [6]  29.39560557    0.13439712    6.21001726    7.30871208   11.02639335+
[11]   3.46749483+  11.81756981+   5.92572203+   1.27107884+   3.50937029+
[16]   0.57383072+  18.08294179    4.31569452+   8.40650219+   0.67590079
[21]   5.37792573    3.17251892+  25.31832664    0.04645629    2.33813901
[26]   5.56691783   12.45000875    3.03198619+   6.97528551    3.90074501+
[31]   3.66245899+   3.25764828+  10.68035229+   4.13541010    2.07197503
[36]  23.61660189   15.28222609  116.22779244    8.27404947+  22.99903182+

> stat.coxph <-
+   aCGH.test(colorectal, surv.obj, test = "coxph",
+         p.adjust.method = "fdr")
> stat.coxph[1:10 ,]

     index  teststat        rawp      adjp
1881  1881  3.090001 0.002001560 0.6706531
1925  1925  3.074021 0.002111948 0.6706531
1886  1886  2.950780 0.003169726 0.6706531
1896  1896  2.865492 0.004163617 0.6706531
1895  1895  2.857561 0.004269112 0.6706531
1319  1319 -2.799944 0.005111142 0.6706531
1227  1227 -2.786826 0.005322712 0.6706531
1798  1798 -2.785977 0.005336669 0.6706531
1924  1924  2.779697 0.005440972 0.6706531
1889  1889  2.769591 0.005612678 0.6706531
```

```
> plotFreqStat(colorectal, stat.coxph, events, titles =
+               c("Survived/Censored", "Dead"), X = FALSE, Y = FALSE)
```

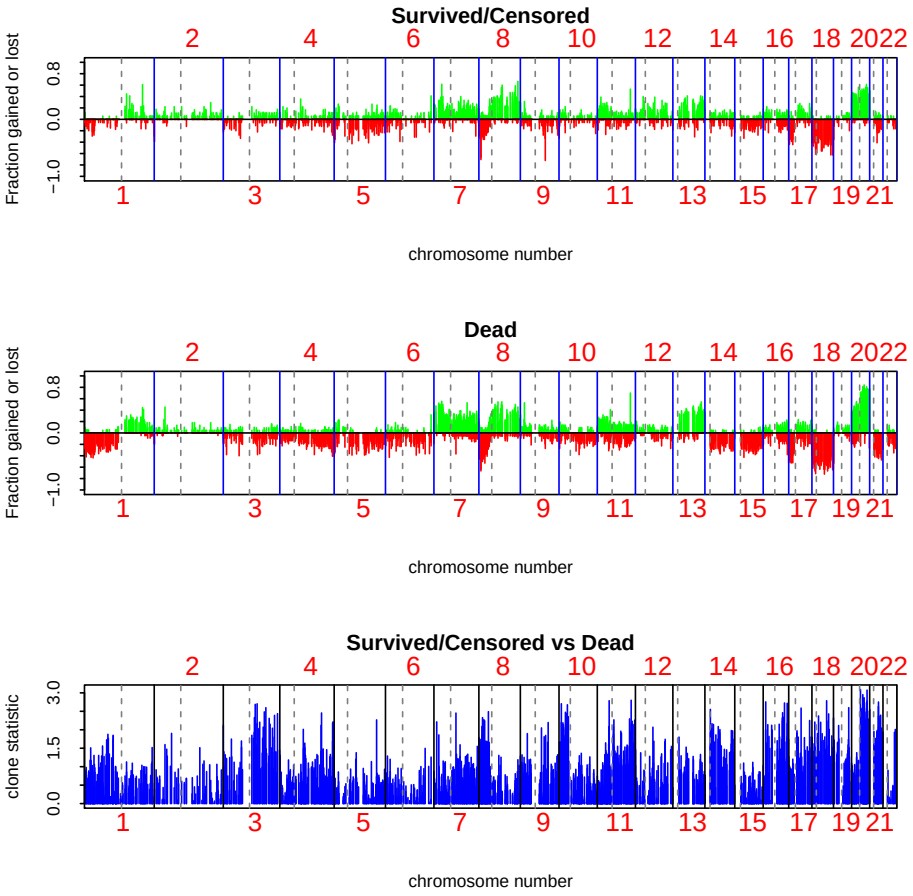

Figure 9: Frequency plots of the samples with respect to survival.

Deriving statistics and p-values for testing the linear association of age with the log2 ratios of each clone along the tumors. Here we repeat above two examples but using significance of linear regression coeffecient as a mesuare of association between genomic variable and continious outcome.

```
> age <- phenotype(colorectal)$age
> age.na <- which(!is.na(age))
> age <- age[age.na]
> colorectal.na <- colorectal[, age.na]
> stat.age <-
+   aCGH.test(colorectal.na, age, test = "linear.regression",
+             p.adjust.method = "fdr")
> stat.age[1:10 ,]
```

```
      index  teststat        rawp       adjp
1735   1735  3.259187 0.002399741 0.9952687
1739   1739  3.184326 0.002941084 0.9952687
685     685 -3.158061 0.003157117 0.9952687
1251   1251  3.144471 0.003274723 0.9952687
1718   1718  3.118281 0.003513183 0.9952687
1714   1714  3.112281 0.003570080 0.9952687
642     642 -3.082287 0.003867826 0.9952687
639     639 -3.012157 0.004658116 0.9952687
643     643 -2.937882 0.005659632 0.9952687
1744   1744  2.881404 0.006552898 0.9952687
```

```
> plotFreqStat(colorectal.na, stat.age, ifelse(age < 70, 0, 1), titles =
+               c("Young", "Old"), X = FALSE, Y = FALSE)
```

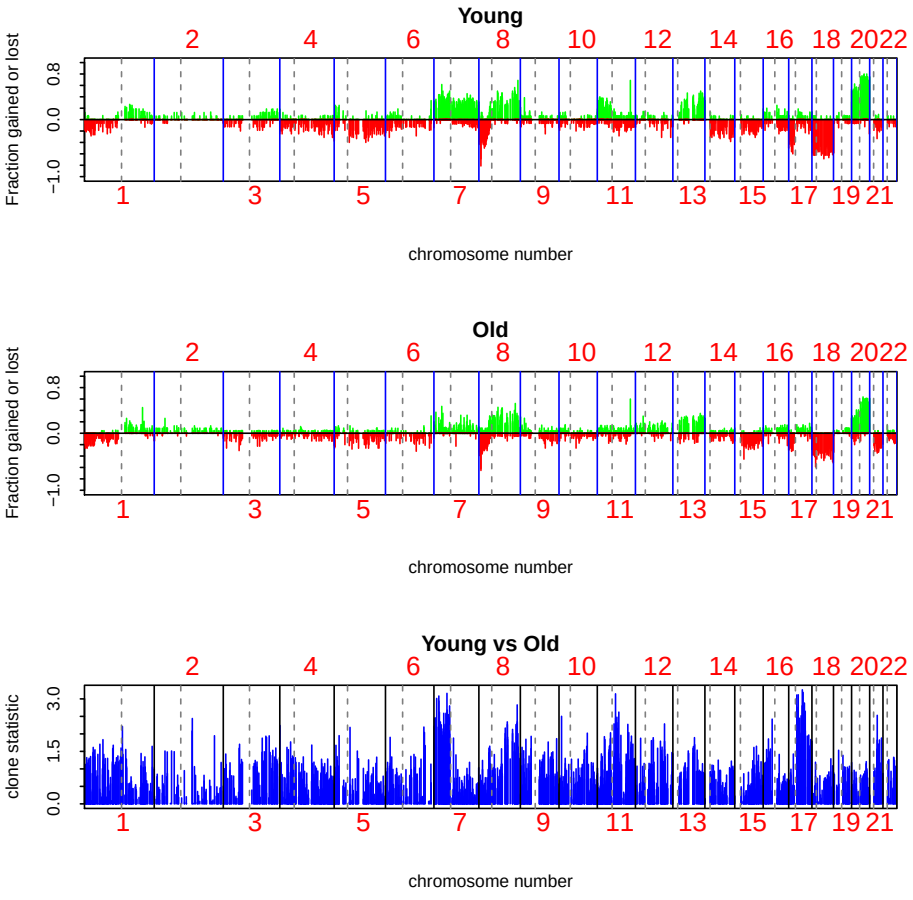

Figure 10: Frequency plots of the samples with respect to age.

Here we show example of how to create a table of results which can be later exported into other programs via *write.table*. First, Males vs Females:

```
> sex <- phenotype(colorectal)$sex
> sex.na <- !is.na(sex)
> index.clones.use <- which(clones.info(colorectal.na)$Chrom < 23)
> colorectal.na <- colorectal[ index.clones.use,sex.na , keep=TRUE]
> dat <- log2.ratios.imputed(colorectal.na)
> resT.sex <- mt.maxT(dat, sex[sex.na], test = "t.equalvar", B = 1000)

b=10        b=20        b=30        b=40        b=50        b=60        b=70        b=80
b=110        b=120        b=130        b=140        b=150        b=160        b=170        b=
b=210        b=220        b=230        b=240        b=250        b=260        b=270        b=
b=310        b=320        b=330        b=340        b=350        b=360        b=370        b=
b=410        b=420        b=430        b=440        b=450        b=460        b=470        b=
b=510        b=520        b=530        b=540        b=550        b=560        b=570        b=
b=610        b=620        b=630        b=640        b=650        b=660        b=670        b=
b=710        b=720        b=730        b=740        b=750        b=760        b=770        b=
b=810        b=820        b=830        b=840        b=850        b=860        b=870        b=
b=910        b=920        b=930        b=940        b=950        b=960        b=970        b=

> sex.tbl <- summarize.clones(colorectal.na, resT.sex, sex[sex.na], titles = c("Male", "Femal
> sex.tbl[1:5,]

       Clone           Target Chrom   kb NumPresent.All NumGain.All NumLost.All
2 RP11-82D16  HumArray2H11_C9     1 2009             38           4           7
3 RP11-62M23 HumArray2H10_N30     1 3368             34           1           7
4 RP11-111O5 HumArray2H10_B18     1 4262             37           1           9
5  RP11-51B4 HumArray2H10_Q30     1 6069             34           0          10
6 RP11-60J11 HumArray2H10_T30     1 6817             35           1           7
  PropPresent.All PropGain.All PropLost.All NumPresent.Male NumGain.Male
2            0.97         0.11         0.18              23            1
3            0.87         0.03         0.21              20            1
4            0.95         0.03         0.24              23            0
5            0.87         0.00         0.29              19            0
6            0.90         0.03         0.20              20            0
  NumLost.Male PropPresent.Male PropGain.Male PropLost.Male NumPresent.Female
2            5             1.00         0.04         0.22                15
3            5             0.87         0.05         0.25                14
4            7             1.00         0.00         0.30                14
5            7             0.83         0.00         0.37                15
6            4             0.87         0.00         0.20                15
  NumGain.Female NumLost.Female PropPresent.Female PropGain.Female
2              3              2               0.94            0.20
3              0              2               0.88            0.00
4              1              2               0.88            0.07
5              0              3               0.94            0.00
6              1              3               0.94            0.07
  PropLost.Female      stat  rawp adjp
2            0.13 1.3456684 0.185    1
```

```
3            0.14 1.2966513 0.214    1
4            0.14 0.7545065 0.445    1
5            0.20 1.9207531 0.066    1
6            0.20 0.5052960 0.640    1
```

3.12 Clustering samples

Here we cluster samples while displaying phenotypes as well as within phenotypes using chromosomes 4, 8 and 9 and display the phenotype labels, in this case, sex. We also indicate high level amplifications and 2-copy deletions with yellow and blue colors. (fig. 11).

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```
> par(mfrow=c(2,1))
> clusterGenome(colorectal.na, response = sex[sex.na],
+                  titles = c("Female", "Male"),
+                  byclass = FALSE, showaber = TRUE, vecchrom = c(4,8,9),
+                  dendPlot = FALSE, imp = FALSE)
> clusterGenome(colorectal.na, response = sex[sex.na],
+                  titles = c("Female", "Male"),
+                  byclass = TRUE, showaber = TRUE, vecchrom = c(4,8,9),
+                  dendPlot = FALSE, imp = FALSE)
>
```

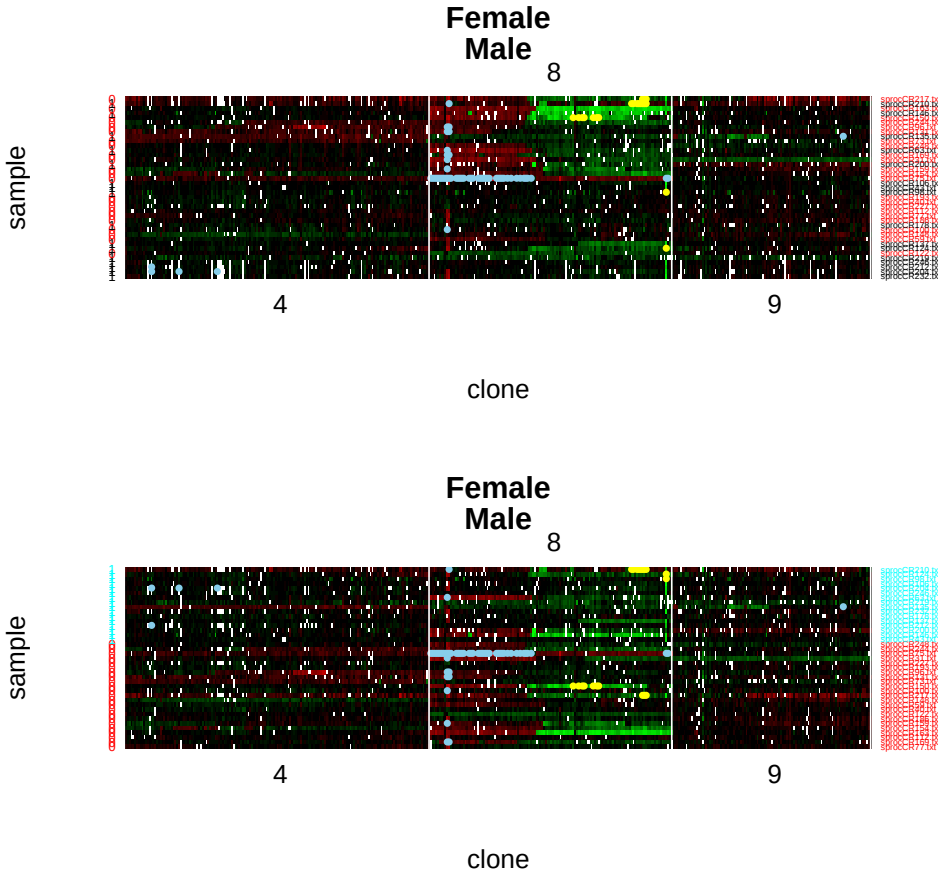

Figure 11: Clustering of the samples by sex