

Bioconductor's aCGH package

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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)
```

```
Loading required package: cluster
```

```
Loading required package: repeated
```

```
Loading required package: rmutl
```

```
Loading required package: rmutl
```

```
Loading required package: survival
```

```
Loading required package: splines
```

```
Loading required package: multtest
```

```
Loading required package: Biobase
```

```
Welcome to Bioconductor
```

```
  Vignettes contain introductory material.  To view,
```

```
  simply type: openVignette()
```

```
  For details on reading vignettes, see
```

```
  the openVignette help page.
```

```
Loading required package: genefilter
```

```
Loading required package: reposTools
```

```
Loading required package: sma
```

```
Attaching package 'aCGH':
```

```
  The following object(s) are masked from package:stats :
```

```
  heatmap
```

```
> 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 of 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 = 0.25, sample.quality.threshold = 0.4, unmapScreen = TRUE,
+   dupRemove = FALSE)
```

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)
```

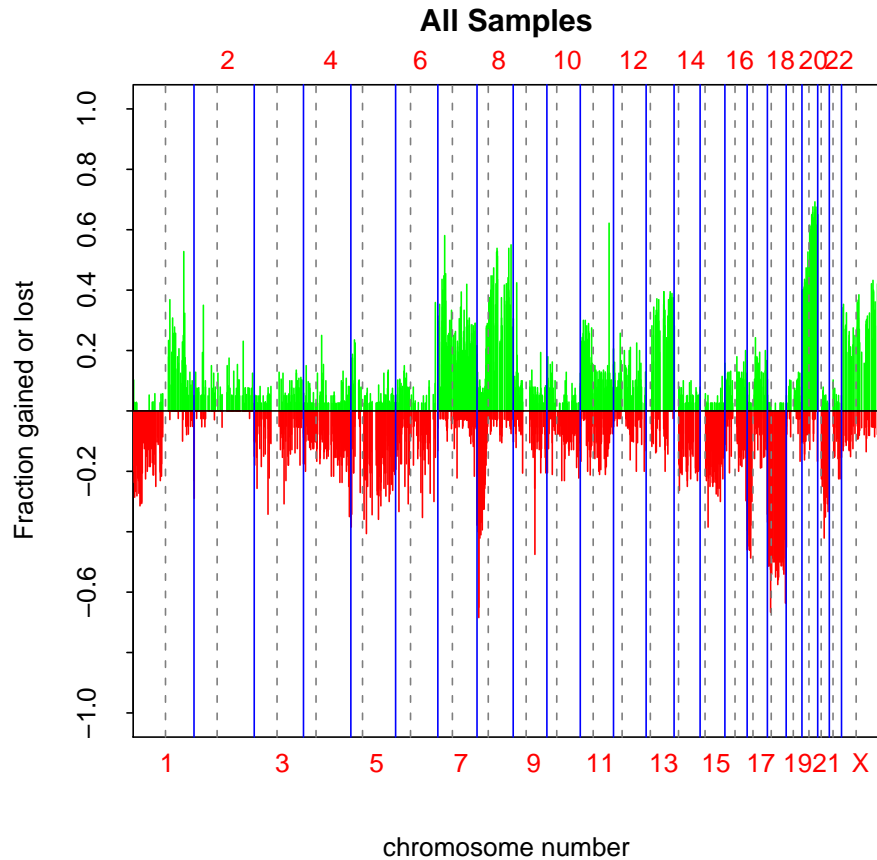


Figure 1: Basic Frequency Plot

```
> 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	gstml	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 = paste("*",
+   "*sproc*", sep = "."), full.names = TRUE), latest.mapping.file,
+   chrom.remove.threshold = 23)
```

```
Trying to read /homes/madman/R-2.0.0/library/aCGH/examples/sprocCR40.txt
Trying to read /homes/madman/R-2.0.0/library/aCGH/examples/sprocCR43.txt
```

Averaging duplicated clones

CTB-102E19	751	752
CTB-112F7	1827	1828
CTB-142024	1774	1775
CTB-339E12	1767	1768
CTB-36F16	1328	1329
CTD-2231J3	2066	2067
GS1-20208	718	719
RP1-97B16	283	284
RP11-119J20	439	440
RP11-13C20	172	173
RP11-149G12	894	895

RP11-172D2	907 908
RP11-175H20	900 901
RP11-176L22	202 203
RP11-188C10	896 897
RP11-1L22	166 167
RP11-204M16	861 862
RP11-20K4	1319 1320
RP11-221P7	902 903
RP11-238H10	935 936
RP11-23G2	195 196
RP11-247E23	197 198
RP11-261B20	483 484
RP11-268N2	892 893
RP11-30M1	185 186
RP11-31B6	2027 2028
RP11-39A8	177 178
RP11-47E6	189 190
RP11-72C6	1098 1099
RP11-81L7	152 153
RP11-83O14	898 899
RP11-94M13	960 961
RP11-99M6	905 906

```
> ex.acgh
```

```
aCGH object
```

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

```
Number of Arrays 2
```

```
Number of Clones 2102
```

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

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

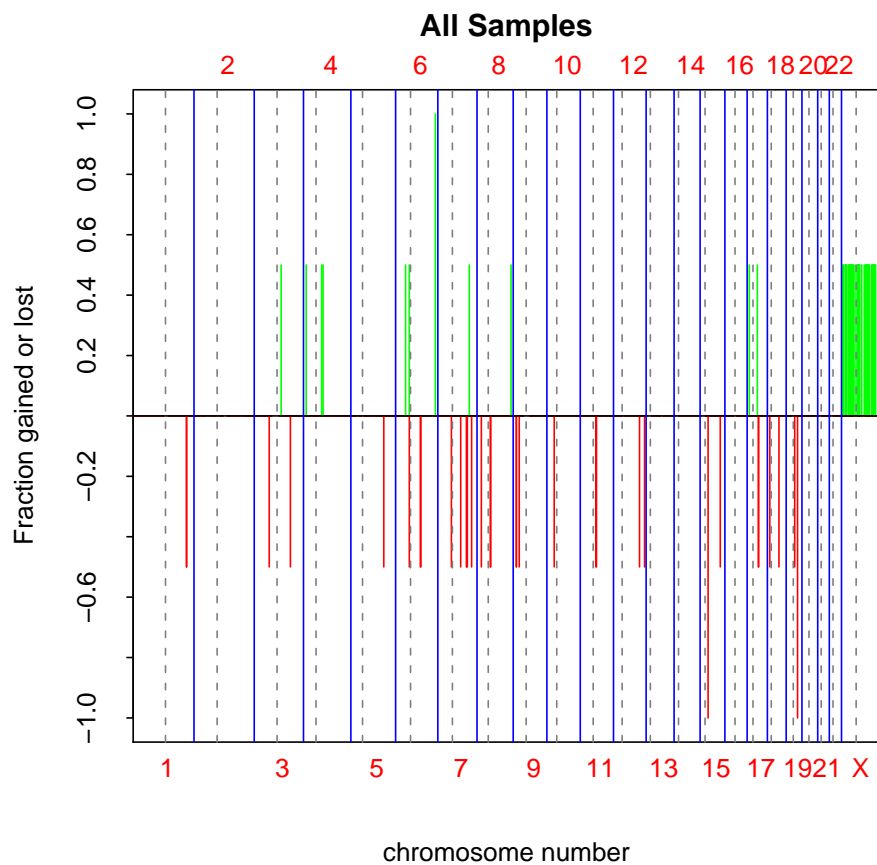


Figure 2: Basic plot for batch of aCGH Sproc files

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 explicitly excluded.

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

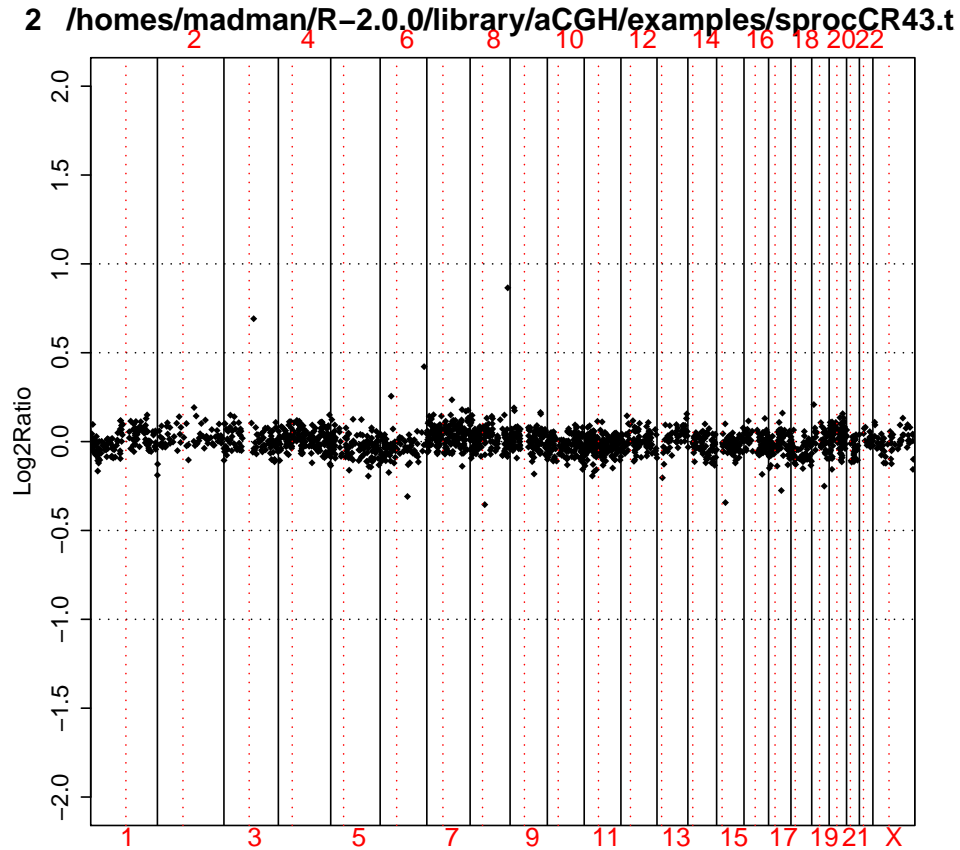


Figure 3: Basic plot for the ordered log2 ratios along the genome

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 using model 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 should 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.

```
> hmm(ex.acgh) <- ex.acgh.hmm
> hmm.merged(ex.acgh) <- mergeHmmStates(ex.acgh, model.use = 1,
+   minDiff = 0.25)
> sd.samples(ex.acgh) <- computeSD.Samples(ex.acgh)
> 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
```

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

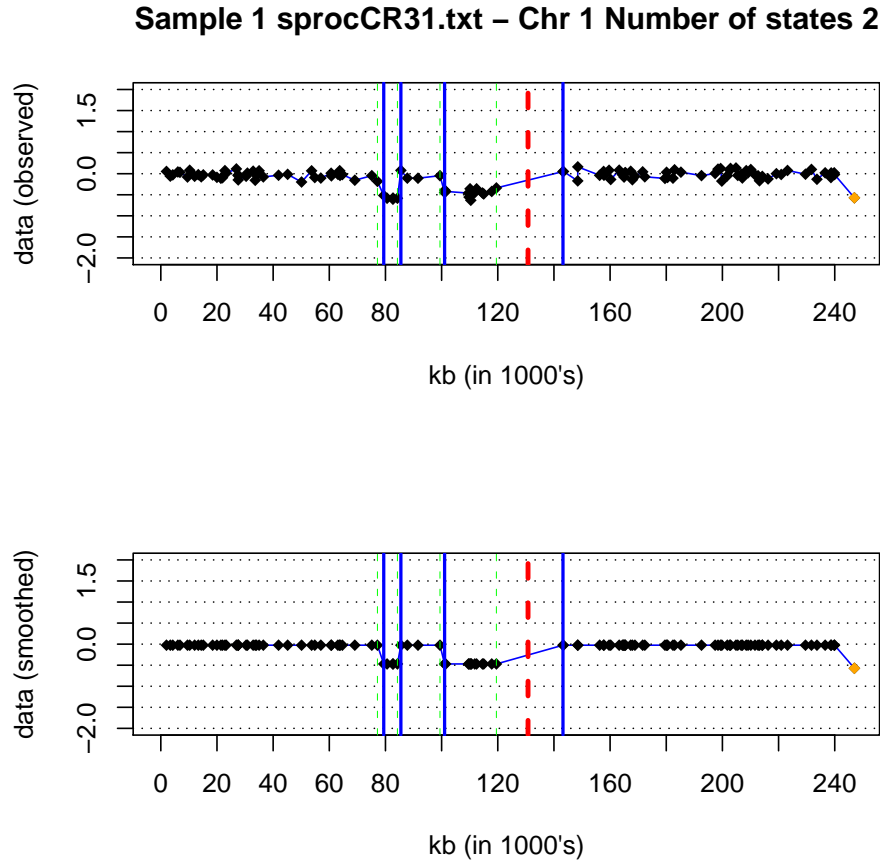


Figure 4: Plotting the hmm states found for colorectal data set.

3.9 Plotting summary of the tumor profiles(fig. ??)

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)
```

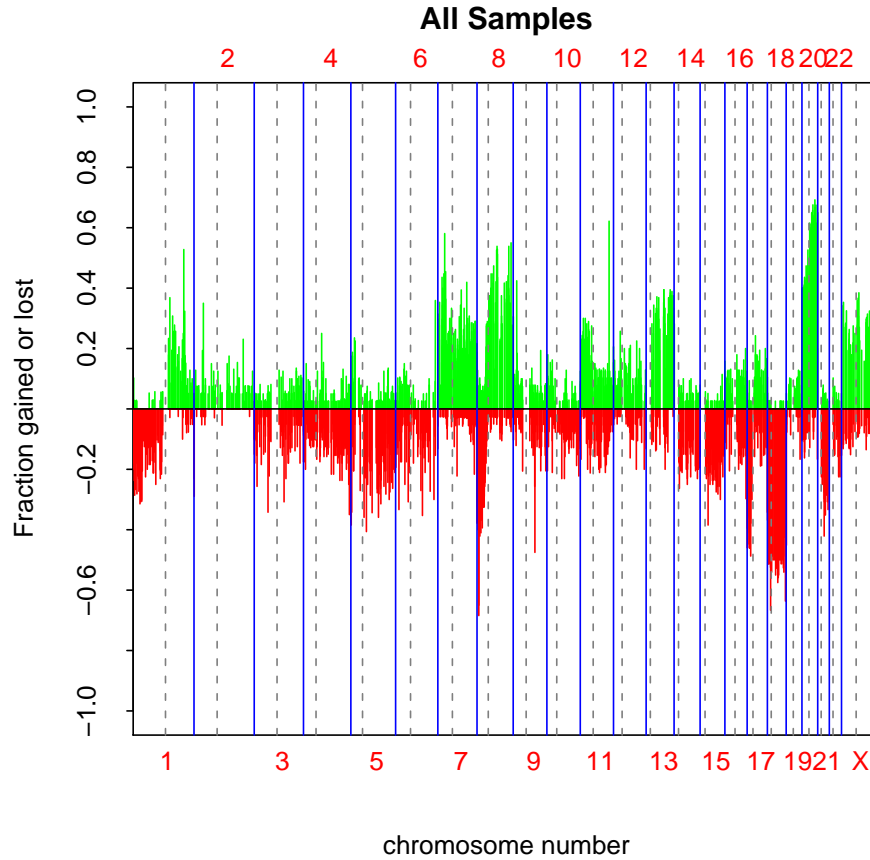


Figure 5: Overall frequency plot of the tumor profiles

`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	RP11-11105	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	RP11-19901	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		

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 as height of the statistic corresponding 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=180	b=190
b=210	b=220	b=230	b=240	b=250	b=260	b=270	b=280	b=290
b=310	b=320	b=330	b=340	b=350	b=360	b=370	b=380	b=390
b=410	b=420	b=430	b=440	b=450	b=460	b=470	b=480	b=490
b=510	b=520	b=530	b=540	b=550	b=560	b=570	b=580	b=590
b=610	b=620	b=630	b=640	b=650	b=660	b=670	b=680	b=690
b=710	b=720	b=730	b=740	b=750	b=760	b=770	b=780	b=790
b=810	b=820	b=830	b=840	b=850	b=860	b=870	b=880	b=890
b=910	b=920	b=930	b=940	b=950	b=960	b=970	b=980	b=990

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

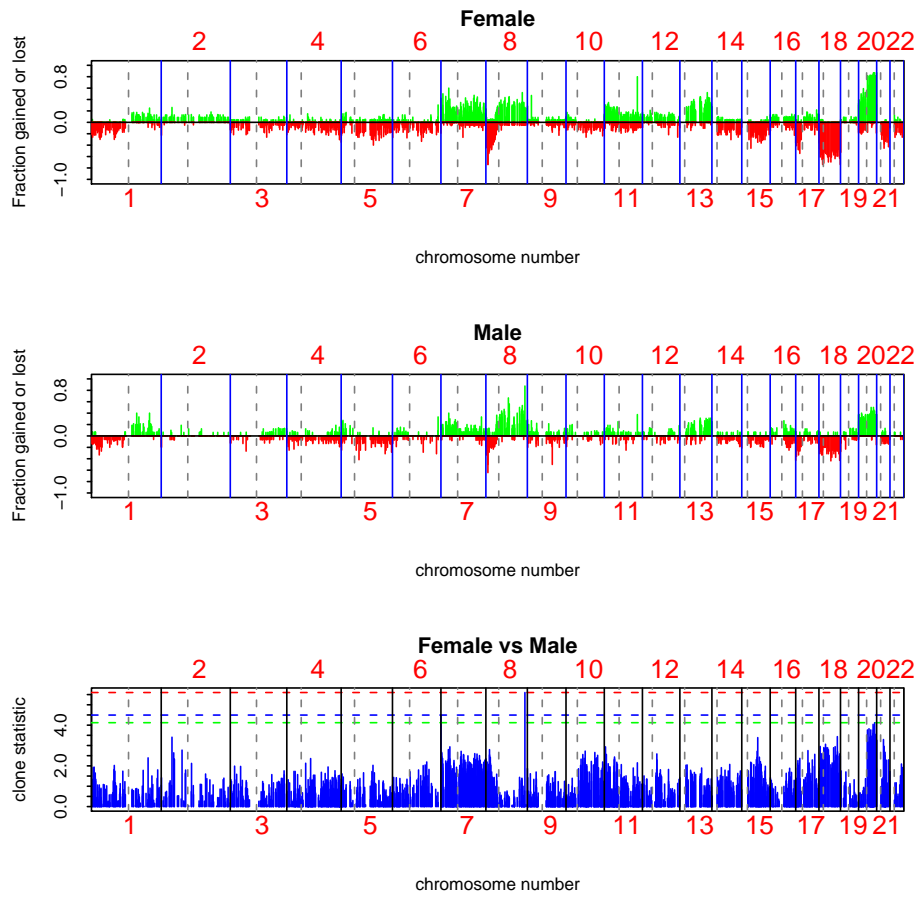
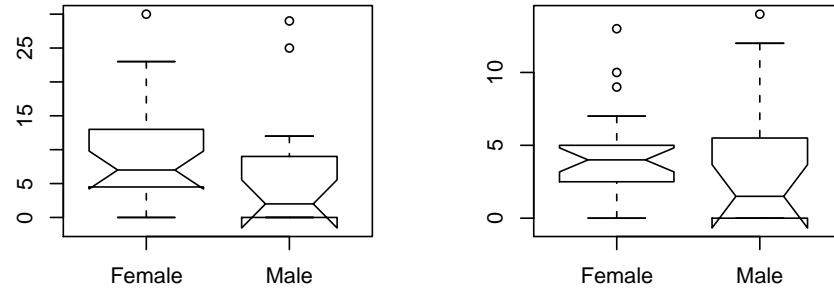


Figure 6: Frequency plots of the samples with respect to the sex groups

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

Number of Transitions 0.0950684 | Number of Chrom containing Transitions (



Number of Aberrations 0.841381 | Number of Whole Chrom Changes 0.01

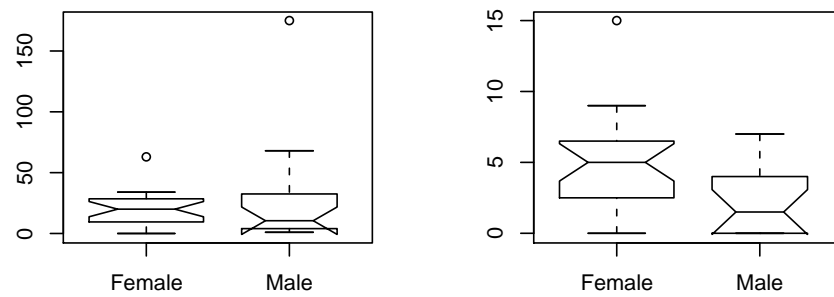


Figure 7: Plotting summary of the tumor profiles

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 subsetting 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 = (factor * (sd.samples(colorectal)$madGenome))[sex.na])
> ind.clones.use <- which(gainloss$gainP >= minChanged | gainloss$lossP >=
+   minChanged & clones.info(colorectal)$Chrom < 23)
> 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=180	b=190
b=210	b=220	b=230	b=240	b=250	b=260	b=270	b=280	b=290
b=310	b=320	b=330	b=340	b=350	b=360	b=370	b=380	b=390
b=410	b=420	b=430	b=440	b=450	b=460	b=470	b=480	b=490
b=510	b=520	b=530	b=540	b=550	b=560	b=570	b=580	b=590
b=610	b=620	b=630	b=640	b=650	b=660	b=670	b=680	b=690
b=710	b=720	b=730	b=740	b=750	b=760	b=770	b=780	b=790
b=810	b=820	b=830	b=840	b=850	b=860	b=870	b=880	b=890
b=910	b=920	b=930	b=940	b=950	b=960	b=970	b=980	b=990

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

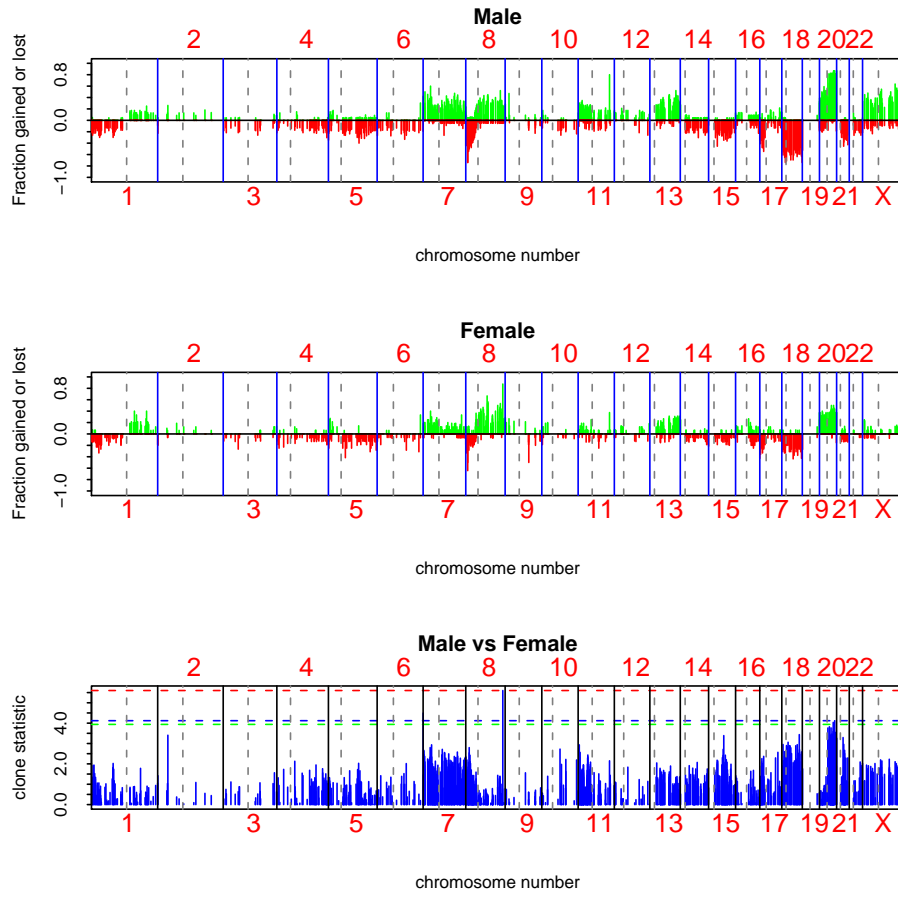


Figure 8: Frequency plots of the samples with respect to the sex groups for clones gained or lost in at least 10% of the samples

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 separated 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 = 0.5)
> surv.obj <- Surv(time, events)
> surv.obj
```

```
[1] 2.0272560 12.7437186+ 15.3348220 8.6675932+ 25.7487609 2.8790693+
[7] 6.8665314+ 29.1389512+ 5.3466401 4.3327062 6.5597736+ 23.1815945+
[13] 20.8710452 1.5970891 14.1588384 25.8791874 1.2191874+ 0.9113252
[19] 1.2203817 45.5021793+ 4.2761491+ 6.2000023+ 5.7578330 1.4165231+
[25] 7.9990727 26.6755137+ 5.5965863 23.6050332+ 17.7456877+ 0.7391386
[31] 22.9690254 3.5503822+ 8.9961451 2.9048886+ 0.1586289+ 6.9715818
[37] 23.7358065+ 15.1973651+ 0.2195054 5.9066016+
```

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

	index	teststat	rawp	adjp
1309	1309	-3.572339	0.0003538068	0.3028515
1342	1342	3.563529	0.0003659020	0.3028515
1287	1287	-3.443085	0.0005751190	0.3028515
1363	1363	3.433220	0.0005964580	0.3028515
1366	1366	3.369973	0.0007517546	0.3053627
1259	1259	-3.259597	0.0011157068	0.3541969
1369	1369	3.229570	0.0012397647	0.3541969
1368	1368	3.195650	0.0013951625	0.3541969
1360	1360	2.992724	0.0027649942	0.4803748
1329	1329	-2.989608	0.0027933525	0.4803748

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

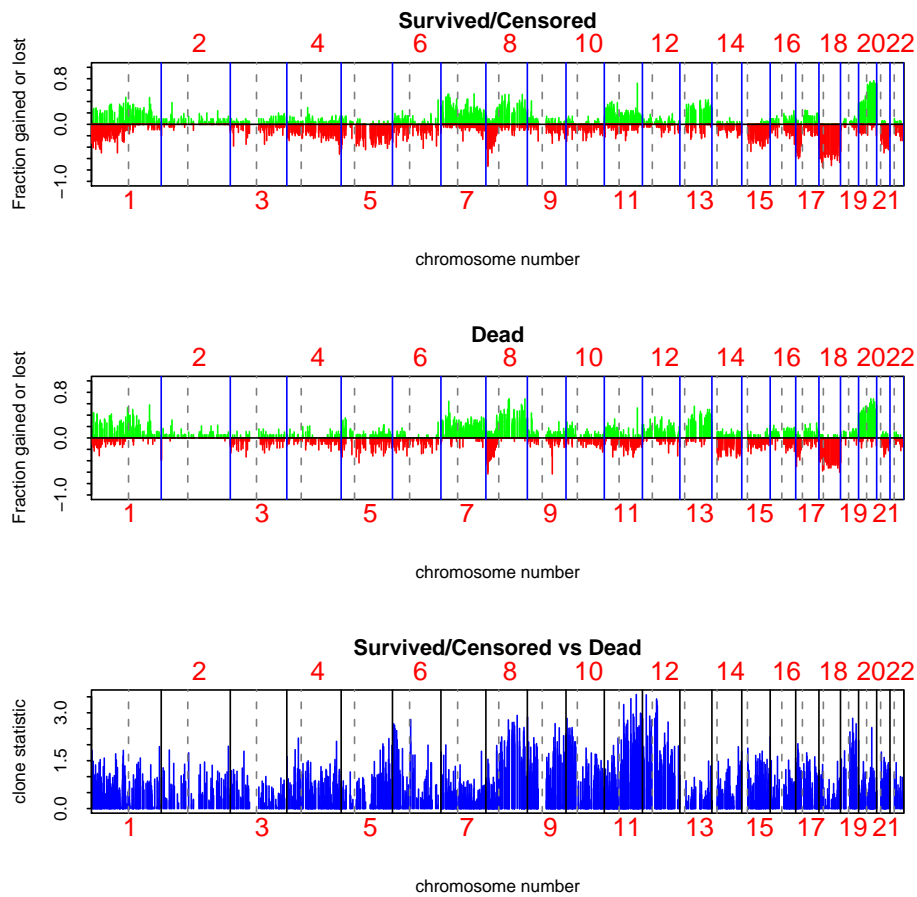


Figure 9: Frequency plots of the samples with respect to survival.

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 coefficient as a measure of association between genomic variable and continuous 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)

```

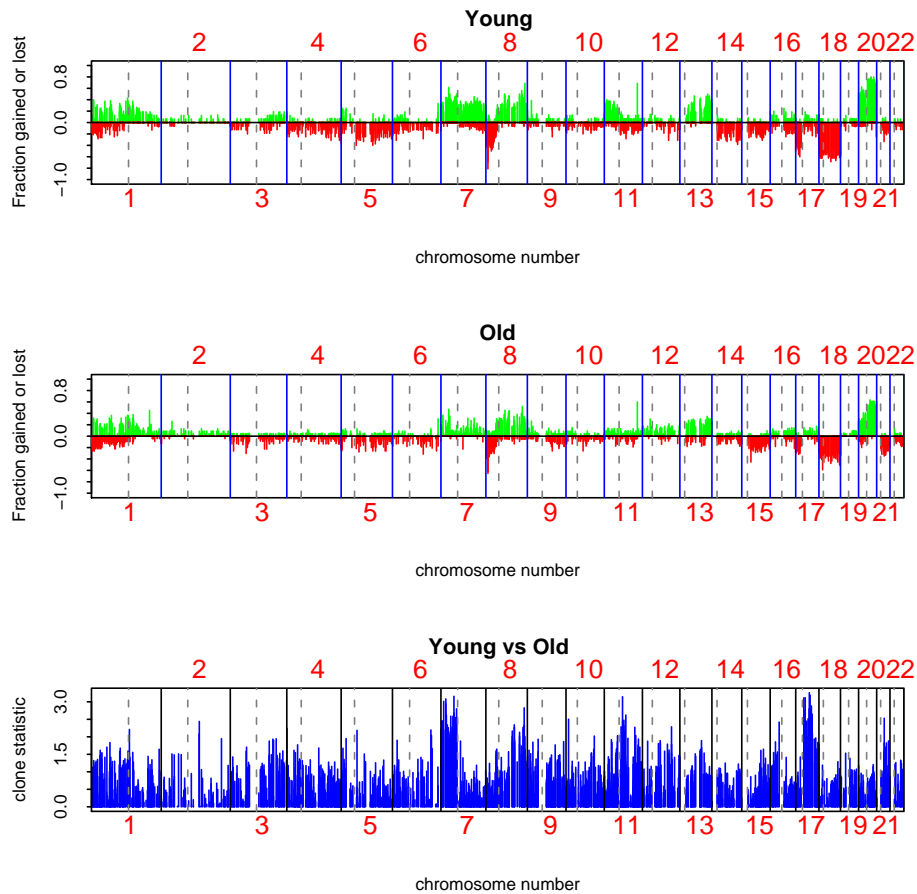


Figure 10: Frequency plots of the samples with respect to age.

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=180	b=190
b=210	b=220	b=230	b=240	b=250	b=260	b=270	b=280	b=290
b=310	b=320	b=330	b=340	b=350	b=360	b=370	b=380	b=390
b=410	b=420	b=430	b=440	b=450	b=460	b=470	b=480	b=490
b=510	b=520	b=530	b=540	b=550	b=560	b=570	b=580	b=590
b=610	b=620	b=630	b=640	b=650	b=660	b=670	b=680	b=690
b=710	b=720	b=730	b=740	b=750	b=760	b=770	b=780	b=790
b=810	b=820	b=830	b=840	b=850	b=860	b=870	b=880	b=890
b=910	b=920	b=930	b=940	b=950	b=960	b=970	b=980	b=990

```
> sex.tbl <- summarize.clones(colorectal.na, resT.sex, sex[sex.na],
+ titles = c("Male", "Female"))
> 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	RP11-11105	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	NumLost.Male	NumPresent.Female
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	NumGain.Female	NumLost.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
	PropPresent.Female	PropGain.Female	PropLost.Female	stat	raup	adjp	
2	0.94	0.20		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).

```
> 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)
```

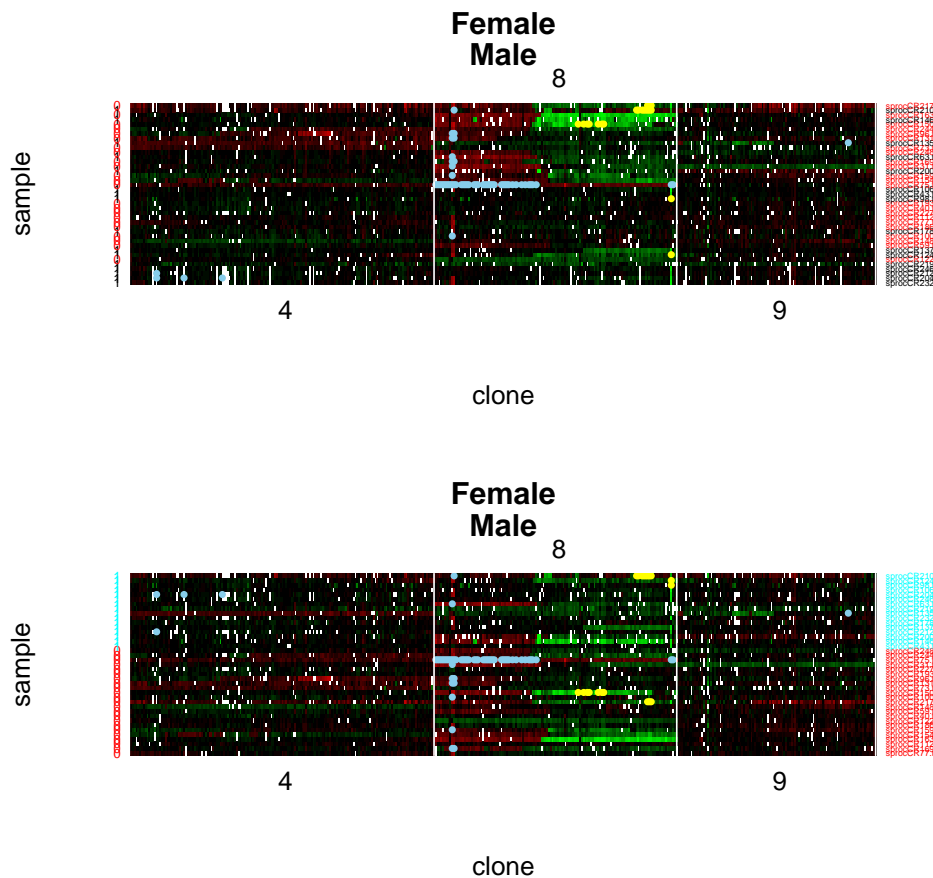


Figure 11: Clustering of the samples by sex

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