

sequenza possible SNP-array usage example

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1 Working with SNP array data

```
> library(sequenza)
```

1.1 Preparing the data

```
> data(BAF)
> data(logR)

> sample.i <- data.frame(chromosome = BAF$chrs, n.base = BAF$pos,
+                         Bf = BAF$S1, adjusted.ratio = logR$S1,
+                         depth.sample = 1, good.s.reads = 1,
+                         ref.zygosity = 'hom', stringsAsFactors = FALSE)
```

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1.1.1 Correcting logR with a normal sample, or with the mean logR value

Without a reference sample (normal germline sample) we can try to divide for the mean value. It would be correct to use the germline logR.

```
> #sample.i$adjusted.ratio <- 2^(sample.i$adjusted.ratio)
> #sample.i$adjusted.ratio <- sample.i$adjusted.ratio / mean(sample.i$adjusted.ratio)
> sample.i$adjusted.ratio <- 2^(sample.i$adjusted.ratio/0.55)
>
```

1.1.2 Retrieve the homozygous position

It should be available a germline sample to get the heterozygous SNP, doing in the same sample it's a risk if the sample is pure. A threshold around 0.25 or 0.35 can be picked to subset the heterozygous position on the germline. In the example we are lowering the threshold while taking the SNP from the same aberrant sample.

```
> het.lim <- 0.2
> is.het <- sample.i$Bf >= het.lim & sample.i$Bf <= 1 - het.lim
> sample.i$ref.zygosity[is.het] <- 'het'
> sample.i$Bf[sample.i$Bf >= 0.5] <- 1 - sample.i$Bf[sample.i$Bf >= 0.5]
> sample.het.i <- sample.i[is.het, ]
```

1.2 Windowing logR values.

```
> snp.r.win <- windowValues(x = sample.i$adjusted.ratio,
+                           positions = sample.i$n.base,
+                           chromosomes = sample.i$chromosome,
+                           window = 1e6, overlap = 1)
```

1.3 Windowing B-allele frequencies values.

```
> snp.b.win <- windowValues(x = sample.het.i$Bf,
+                           positions = sample.het.i$n.base,
+                           chromosomes = sample.het.i$chromosome,
+                           window = 1e6, overlap = 1)
```

1.4 Chromosome view without mutation

```
> chromosome.view(baf.windows = snp.b.win[[1]],  
+               ratio.windows = snp.r.win[[1]],  
+               min.N.ratio = 1)
```

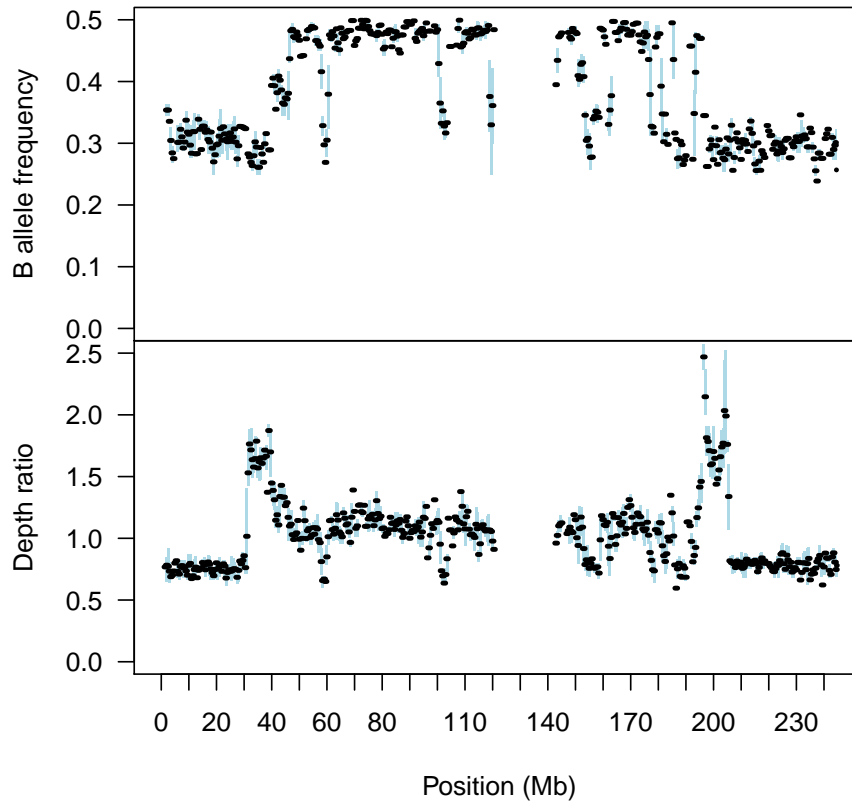


Figure 1: Plots B-allele frequencies (top) and un-logged-logR (bottom) with SNP array data.

1.5 Segmenting with the *copynumber* package

```
> breaks <- find.breaks(sample.het.i, gamma = 20, kmin = 15, baf.thres = c(0, 0.5))  
> seg.i <- segment.breaks(sample.i, breaks = breaks)
```

1.6 Using the Bayesian inference on segmented SNP arrays

```
> weights.snp    <- 150 + round((seg.i$end.pos - seg.i$start.pos)/1e6 , 0)
> filter.size    <- (seg.i$end.pos - seg.i$start.pos) >= 3e6

> avg.unlogR <- mean(sample.i$adjusted.ratio, na.rm = TRUE)
> CP.snp <- baf.model.fit(Bf = seg.i$Bf[filter.size],
+                          depth.ratio = seg.i$depth.ratio[filter.size],
+                          weight.ratio = weights.snp[filter.size],
+                          weight.Bf = weights.snp[filter.size],
+                          avg.depth.ratio = avg.unlogR,
+                          cellularity = seq(0.1,1,0.01),
+                          dna.index = seq(0.5,3,0.05), mc.cores = 4,
+                          priors.labels = 2, priors.values = 2)

> cint <- get.ci(CP.snp)
> cellularity <- cint$max.y
> dna.index    <- cint$max.x
```

1.7 Cellularity and DNA-index plot for SNP array

```
> cp.plot(CP.snp)
> cp.plot.contours(CP.snp, add = TRUE)
```

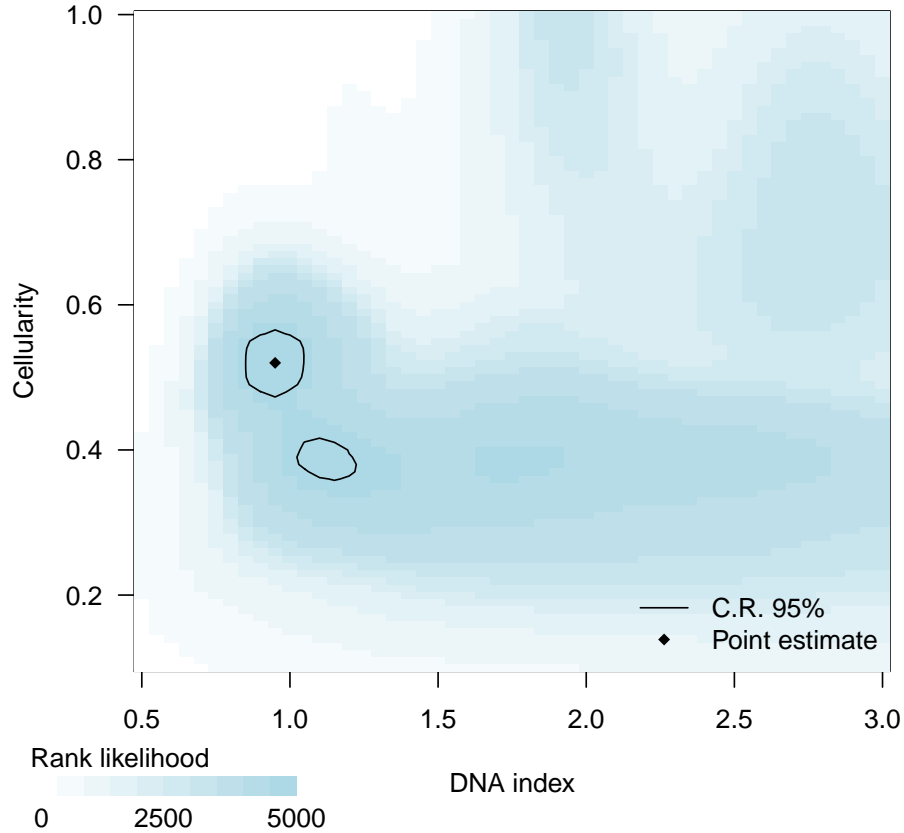


Figure 2: Result from the Bayesian inference over the defined range of cellularity and DNA-index from artificial SNP array data. The color indicate the log-likelihood of the corresponding cellularity/DNA-index combinations.

1.8 Call for copy number variation using inferred parameters.

```
> snp.seg.cn <- baf.bayes(Bf = seg.i$Bf,
+                          depth.ratio = seg.i$depth.ratio,
+                          avg.depth.ratio = avg.unlogR,
+                          cellularity = cellularity,
+                          weight.ratio = 2 * 300,
```

```

+           weight.Bf = 300, ratio.priority = FALSE,
+           dna.index = dna.index, CNt.max = 10)
> segmented.snp <- cbind(seg.i, snp.seg.cn)
> head(segmented.snp[segmented.snp$chromosome == 1, ])

```

	chromosome	start.pos	end.pos	Bf	N.BAF	depth.ratio	N.ratio	CNt	A	B
1	1	2189662	30490508	0.3080575	87	0.7538262	134	1	1	0
2	1	31697751	39213527	0.2817625	16	1.6662164	32	5	4	1
3	1	40285096	46296225	0.3786333	21	1.2857143	32	3	2	1
4	1	46437972	55282671	0.4791852	27	1.0502976	37	2	1	1
5	1	55913726	61908401	0.4126143	14	0.9321436	20	2	1	1
6	1	62012795	100351185	0.4781943	70	1.1108629	121	2	1	1

L

```

1 -14.81364
2 -16.11271
3 -14.96024
4 -14.55974
5 -20.11385
6 -14.83635

```

1.9 Graphical representation of copy number with SNP arrays

```
> chromosome.view(baf.windows = snp.b.win[[1]],  
+               ratio.windows = snp.r.win[[1]], min.N.ratio = 1,  
+               segments = segmented.snp[segmented.snp$chromosome == "1", ],  
+               cellularity = cellularity, dna.index = dna.index,  
+               avg.depth.ratio = avg.unlogR, main = "1")
```

1

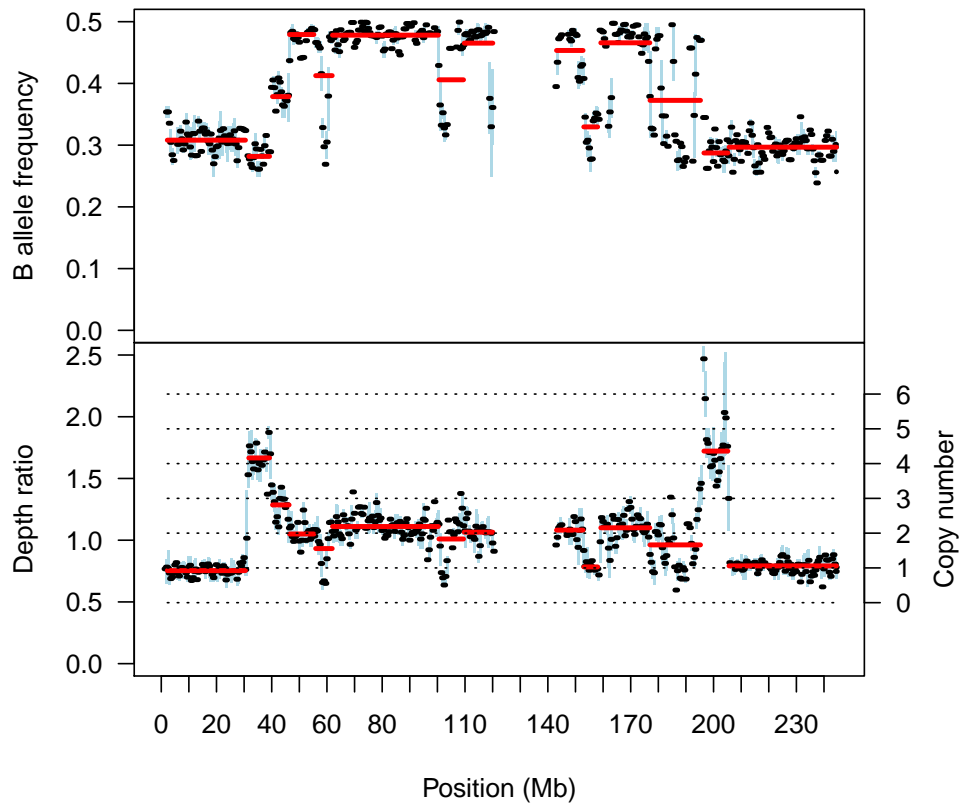


Figure 3: Plots B-allele frequencies (top) and un-logged-logR (bottom) with SNP array data. Chromosome 16. Horizontal dotted line indicate different copy number/ allele state.

```

> chromosome.view(baf.windows = snp.b.win[[16]],
+               ratio.windows = snp.r.win[[16]], min.N.ratio = 1,
+               segments = segmented.snp[segmented.snp$chromosome == "16", ],
+               cellularity = cellularity, dna.index = dna.index,
+               avg.depth.ratio = avg.unlogR, main = "16")

```

16

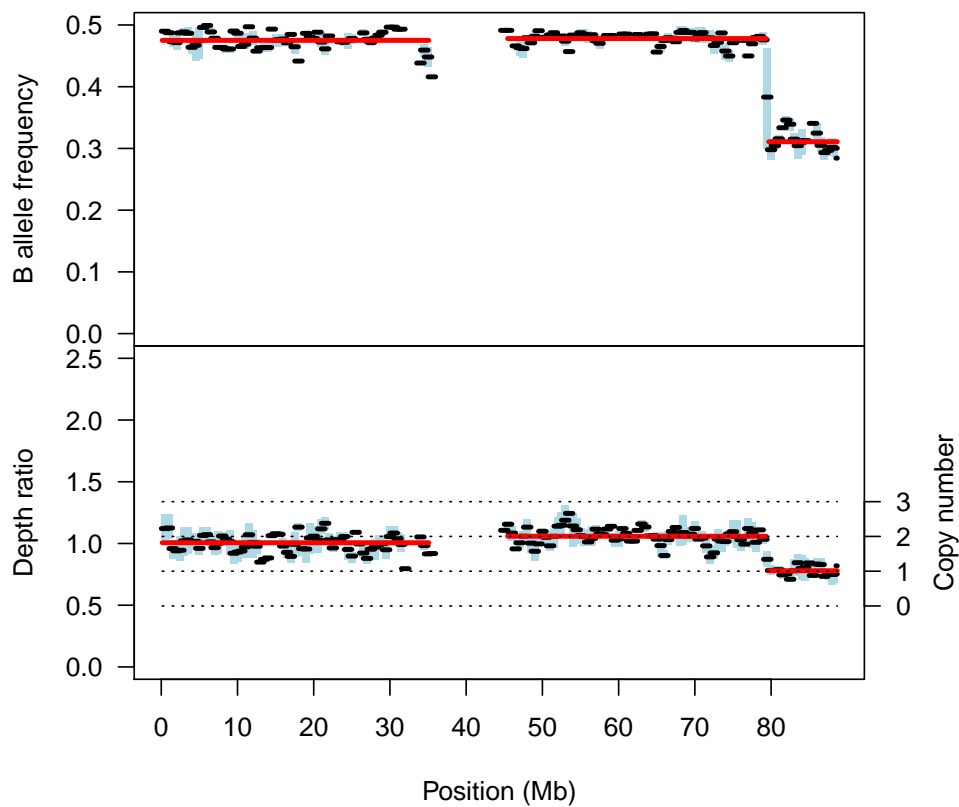


Figure 4: Plots B-allele frequencies (top) and un-logged-logR (bottom) with SNP array data. Chromosome 16. Horizontal dotted line indicate different copy number/ allele state.


```
> genome.view(seg.cn = segmented.snp, info.type = "CNt")
> legend("bottomright", bty="n", c("Tumor copy number"), col = c("red"),
+       inset = c(0, -0.4), pch=15, xpd = TRUE)
```

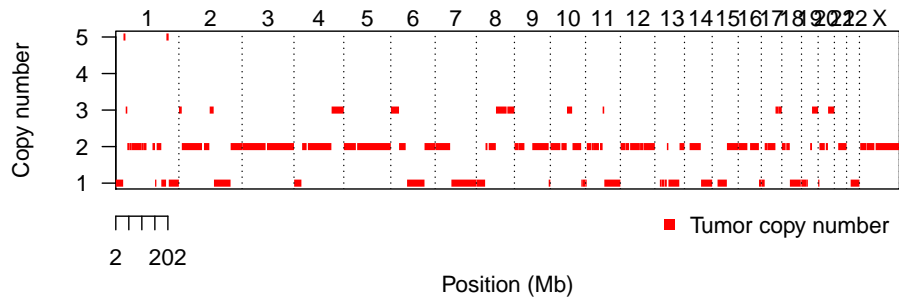


Figure 5: Genome wide copy number profile obtained from one SNP array.

```
> genome.view(seg.cn = segmented.snp, info.type = "AB")
> legend("bottomright", bty = "n", c("A-allele", "B-allele"), col= c("red", "blue"),
+       inset = c(0, -0.45), pch = 15, xpd = TRUE)
```

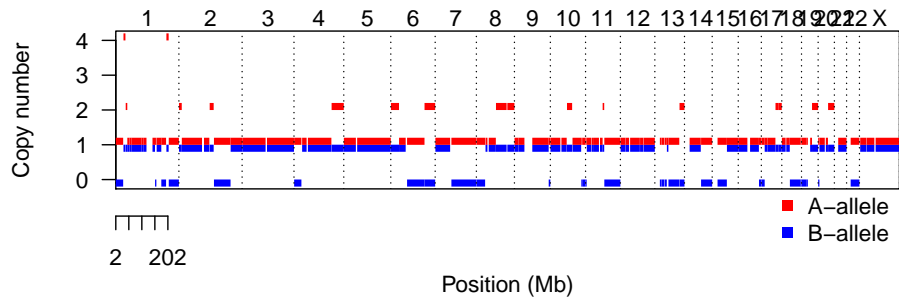


Figure 6: Genome wide A and B alleles profile, obtained from one SNP array.