Tools for high throughput SNP chip data

Robert Scharpf, Jonathan Pevsner, Jason Ting, and Ingo Ruczinski July 13, 2007

Introduction

SNPchip defines classes and methods useful for organizing high throughput genomic data. The classes defined here extend the eSet class in *Biobase*, utilizing the existing Bioconductor infrastructure for organizing high dimensional genomic data. This provides a foundation upon which statistical and visualization tools can be further developed.

1 Simple Usage

We illustrate the structure of the class AnnotatedSnpSet with a small dataset provided with the package.

```
> options(width = 69)
> library(SNPchip)
> data(annSnpset)
> annSnpset
AnnotatedSnpSet (storageMode: lockedEnvironment)
assayData: 5896 features, 5 samples
  element names: calls, callsConfidence, cnConfidence, copyNumber
phenoData
An object of class "AnnotatedDataFrame"
  sampleNames: NA17101_X_hAF_A1_4000091.CEL, NA17102_X_hAF_A2_4000091
  .CEL, ..., NA17105_X_hAF_A5_4000091.CEL (5 total)
  varLabels and varMetadata description: none
featureData
An object of class "AnnotatedDataFrame"
  rowNames: SNP_A-1507972, SNP_A-1641761, ..., SNP_A-1759046 (5896 total)
  varLabels and varMetadata description:
    dbsnp_rs_id: dbsnp_rs_id
    chrom: chrom
    ...: ...
    enzyme: enzyme
    (8 total)
experimentData: use 'experimentData(object)'
Annotation [1] "pd.mapping50k.xba240"
chromosomeAnnotation
   centromereStart centromereEnd chromosomeSize
         121147476
                       123387476
                                      245522847
2
          91748045
                        94748045
                                      243018229
```

3	90587544	93487544	199505740
4	49501045	52501045	191411218
5	46441398	49441398	180857866
6	58938125	61938125	170975699
7	57864988	60864988	158628139
8	43958052	46958052	146274826
9	46035928	49035928	138429268
10	39244941	41624941	135413628
11	51450781	54450781	134452384
12	34747961	36142961	132449811
13	16000000	17868000	114142980
14	15070000	18070000	106368585
15	15260000	18260000	100338915
16	35143302	36943302	88827254
17	22187133	22287133	78774742
18	15400898	16764896	76117153
19	26923622	29923622	63811651
20	26267569	28033230	62435964
21	10260000	13260000	46944323
22	11330000	14330000	49554710
X	58465033	61465033	154824264
Y	11237315	12237315	57701691

annSnpset is an instance of the AnnotatedSnpSet class. Here, the assayData slot in AnnotatedSnpSet contains 5896 SNPs with estimates of copy number and genotype calls, as well as a corresponding confidence score. Typically, such an object would contain 100,000 - 500,000 estimates of genotype calls and copy number. We illustrate in Section 3 how to create an instance of AnnotatedSnpSet from probe-level summaries of SNP chip data. In addition to estimates of genotype call and copy number, the annSnpset contains both chromosome-level annotation, as well as SNP-level annotation. The chromosome-level annotation includes the centromere start and stop sites and chromosome size (in number of base pairs), and could be extended to include location of cytobands, or any other feature of a chromosome.

- > data(chromosomeAnnotation)
- > chromosomeAnnotation[1:5,]

	${\tt centromereStart}$	${\tt centromereEnd}$	chromosomeSize
1	121147476	123387476	245522847
2	91748045	94748045	243018229
3	90587544	93487544	199505740
4	49501045	52501045	191411218
5	46441398	49441398	180857866

The method getSnpAnnotation retrieves SNP-level annotation from annotation packages maintained at Bioconductor. A more rich annotation is in development. The appropriate pd.mapping library needs to be loaded for this method to work.

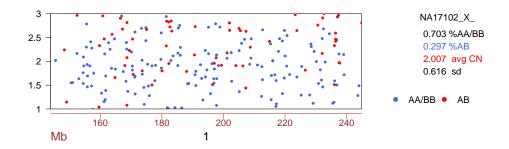
- > annotation(annSnpset)
- > library("pd.mapping50k.xba240")
- > featureData(annSnpset) <- getSnpAnnotation(annSnpset)</pre>

A genome-wide view of copy number and genotype calls versus physical position can be made using plotSnp. Here, we plot chromosomes 1-22 and X (the integer 23 is used to represent X) of samples 1 - 4 in the object annSnpset:

```
> plotSnp(annSnpset, chromosomes = c(1:22, "X"), samples = 1:4,
        width.right = 10, cex.axis = 1, lab = c(3, 3, 5),
        cex.lab = 1.2, cex.legend = c(1, 1.2), legend = c(TRUE,
              FALSE))
              2
                                                                           18 20 22
                                                           12
                                                                 14
                                                                       16
                                                                 50
                                                                       50
                                                                           20 20 30
111 111 111
                                                                                            NA17101_X
                                                                                            0.686 %AA/BE
                                                                                            0.314 %AB
2.010 avg CN
                                                                                            NA17102_X_
                                                                                            0.701 %AA/BE
                                                                                             2.012 avg CN
                                                                                            NA17103_X_
                                                                                            0.686 %AA/BE
                                                                                            0.314 %AB
2.011 avg CN
                                                                                            NA17104_X_
                                                                                            0.682 %AA/BB
                                                                                            2.014 avg CN
```

The copy number estimates have been centered to have mean zero – a centered copy number of 0 corresponds to a copy number of two. The default plot layout generally works well, but can be adjusted through the arguments mar, oma, and width right in plotSnp. The latter argument specifies how much room to allow for the summary panel relative to the size of the smallest chromosome plotted. For instance, if plotting chromosomes 1-22 and X, width right set to 15 allows a plotting region for the summary panel that is 15 times larger than chromosome 21. A more focused view of chromosomes 1, 7, 16, 19, and X of sample 2 could be obtained by

```
> plotSnp(annSnpset, c(1, 7, 16, 19, "X"), c(2, 5), cex = c(1,
+ 1, 1), pch = c(20, 21, 20), bg = c("royalblue",
+ "white", "royalblue"), bty = "o", width.right = 1.6,
+ cex.axis = 1.2, cex.lab = 1.5, cex.legend = c(1.2,
+ 1.2), xaxs = "r")
```

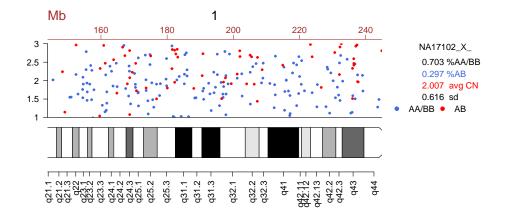


A plot of just the p-arm in sample 2 of chromosome 1:

```
> chr1 <- annSnpset[chromosome(annSnpset) == "1", ]
> start <- min(position(chr1)[position(chr1) > chromosomeAnnotation["1",
```

```
1]], na.rm = TRUE)
 plotSnp(chr1[position(chr1) > start, ], 1, 2, xlim = range(position(chr1)[position(chr1) >
      start], na.rm = TRUE), cex = c(1, 1, 1), pch = c(20, 1)
      20, 20), bg = c("royalblue", "red", "royalblue"),
      bty = "o", width.right = 0.4, cex.axis = 1.2, cex.lab = 1.5,
      cex.legend = c(1.2, 1.2))
   3
                                                            NA17102_X_
                                                             0.703 %AA/BB
  2.5
                                                             0.297 %AB
                                                             2.007 avg CN
   2
                                                             0.616 sd
  1.5
                                                           AA/BB • AB
           160
                     180
                              200
                                       220
                                                240
     Mb
                            1
Cytobands can be added to graphs as follows:
> data(annSnpset)
> data(cytoband)
> chr1 <- annSnpset[chromosome(annSnpset) == "1", ]</pre>
 3, 3), cex.axis = 1.2, cex.legend = c(1.2, 1.2),
      addCytoband = TRUE, legend.location = c("topleft",
          "bottomleft"), height.cytoband = 0.2, width.right = 0.2,
      bty = "o", cex.lab = 1.5, ncol = 1, adj = 0)
     Mb
                                                             NA17105_X_
                                                             0.716 %AA/BB
  2.5
                                                             0.284 %AB
                                                             1.998 avg CN
                                                             0.582 \text{ sd}
                                                              AA/BB
  1.5
                                                              AΒ
> plotSnp(chr1[position(chr1) > start, ], 1, 2, xlim = range(position(chr1)[position(chr1) >
```

> plotSnp(chrl[position(chrl) > start,], 1, 2, xlim = range(position(chrl)[position(chrl)]
+ start], na.rm = TRUE), cex = c(1, 1, 1), pch = c(20,
+ 20, 20), bg = c("royalblue", "red", "royalblue"),
+ bty = "l", width.right = 0.3, cex.axis = 1.2, cex.lab = 1.5,
+ cex.legend = c(1.2, 1.2), addCytoband = TRUE)



2 Available annotation

Bioconductor annotation packages for high throughput SNP platforms are under development. Column headers for the annotation that is currently available for each SNP is here:

> colnames(fData(annSnpset))

We store SNP-level attributes in the featureData slot. The command

> featureData(obj) <- getSnpAnnotation(annSnpset)</pre>

automatically loads the appropriate annotation package according to the annotation slot. The Bioconductor annotation packages must first be downloaded.

Alternatively, one may obtain the NetAffx annotation saved as an R object here:

> colnames(mapping10k\$annotation)

For more detailed annotation on specific SNPs, see the R package RSNPper available at Bioconductor.

3 High throughput SNP classes

All that is needed to create an instance of AnnotatedSnpCallSet or AnnotatedSnpCopyNumberSetis a matrix of genotype calls and copy number, respectively, and their corresponding confidence scores. If estimates of both copy number and genotype calls are available, we can create an AnnotatedSnpSet that inherits methods from both AnnotatedSnpCopyNumberSet and AnnotatedSnpCallSet. In this way, SNPchip is completely independent of the pre-processing method used to produce probe-level summaries. To illustrate, the following code chunk loads a list of matrices obtained from normal subjects in the Hapmap project and pre-processed by CRLMM (B. Carvalho et. al, Biostatistics, in press). Only every 10th SNP from the Xba 50k chip is included in the matrices.

```
> data(hapmap)
> str(hapmap)
```

```
List of 3
$ calls : int [1:5896, 1:5] 2 2 2 3 3 3 1 1 3 3 ...
... attr(*, "dimnames")=List of 2
....$ : chr [1:5896] "SNP_A-1507972" "SNP_A-1641761" "SNP_A-1641781" "SNP_A-1641805" ...
....$ : chr [1:5] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
$ callsConfidence: num [1:5896, 1:5] 566 326 202 668 674 ...
... attr(*, "dimnames")=List of 2
....$ : chr [1:5896] "SNP_A-1507972" "SNP_A-1641761" "SNP_A-1641781" "SNP_A-1641805" ...
....$ : chr [1:5] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
$ copyNumber : num [1:5896, 1:5] 2.67 1.77 2.18 2.08 2.02 ...
... attr(*, "dimnames")=List of 2
....$ : chr [1:5896] "SNP_A-1507972" "SNP_A-1641761" "SNP_A-1641781" "SNP_A-1641805" ...
...$ : chr [1:5] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
```

Each matrix in the list contains probeset summaries (rows) by column (samples). Currently, we only provide annotation for the Affymetrix SNP chips and so the rownames of the matrices should be Affymetrix probeset id's. For purposes of visualization, an identifier from any technology could be used so long as the SNP-level annotation stored in the featureData slot is a data.frame with columns Physical.Position and chromosome.

```
> rownames(hapmap$calls)[1:5]
```

sep = ""))))

```
[1] "SNP_A-1507972" "SNP_A-1641761" "SNP_A-1641781" "SNP_A-1641805"
[5] "SNP_A-1641825"

> rowSds <- function(x) apply(x, 1, "sd")
> colSds <- function(x) apply(x, 2, "sd")
> nr <- nrow(hapmap$copyNumber)
> nc <- ncol(hapmap$copyNumber)
> snpset <- new("AnnotatedSnpSet", calls = hapmap$calls,
+ callsConfidence = hapmap$callsConfidence, copyNumber = hapmap$copyNumber,
+ cnConfidence = matrix(NA, nr, nc), annotation = "pd.mapping50k.xba240",
+ chromosomeAnnotation = chromosomeAnnotation)
> library("pd.mapping50k.xba240")
> annSnpset <- getSnpAnnotation(snpset)</pre>
```

This may take several minutes depending on your internet connection. To do this manually using NetAffx annotation files, the annotation files can be downloaded from

http://biostat.jhsph.edu/ iruczins/publications/sm/2006.scharpf.bioinfo/mapping/. This object should be converted to an object of class AnnotatedDataFrame with SNPs in the same order as in the AnnotatedSnpSet object. To download a static data.frame of the NetAffx annotation for the 50k Xba SNP chip, execute the following command:

Below, we illustrate how one might convert output from Affymetrix CNAT software to an object of class AnnotatedSnpSet. For instance, any one of the .txt files for the CEPH trios provided at the Affymetrix website can be converted as follows

```
> cnat <- read.table("100k_trios.Hind.1.txt", as.is = TRUE,
      sep = "\t", header = TRUE, row.names = 1, skip = 0)
> cn <- as.matrix(cnat[, grep("SPA_CN", colnames(x))])</pre>
> calls <- cnat[, grep("_Call", colnames(x))]</pre>
> calls[calls == "AA"] <- 1
> calls[calls == "AB"] <- 2
> calls[calls == "BB"] <- 3
> calls[calls == "NoCall"] <- 4
> calls <- matrix(as.integer(as.matrix(calls)), nc = dim(calls)[2],
      byrow = FALSE)
> cnConfidence <- as.matrix(cnat[, grep("SPA_pVal", colnames(cnat))])</pre>
> callsConfidence <- as.matrix(cnat[, grep("LOH", colnames(cnat))])</pre>
> rownames(calls) <- rownames(cn) <- x$Probe.Set
> rownames(cnConfidence) <- rownames(callsConfidence) <- x$Probe.Set
> colnames(cn) <- colnames(calls) <- substr(colnames(cn),
> colnames(callsConfidence) <- colnames(cnConfidence) <- substr(colnames(cn),
      1, 7)
> trios <- new("AnnotatedSnpSet", calls = calls, copyNumber = copyNumber,
      callsConfidence = callsConfidence, cnConfidence = cnConfidence,
      annotation = "pd.mapping50k.hind240", chromosomeAnnotation = chromosomeAnnotation)
> library("pd.mapping50k.hind240")
> featureData(trios) <- getSnpAnnotation(trios)</pre>
The SNP-level annotation for the trios data can be retrieved as described previously.
> cnset <- as(annSnpset, "AnnotatedSnpCopyNumberSet")</pre>
> plotSnp(object = cnset, chromosomes = 1:10, samples = 1:3,
      cex = 5, pch = ".", width.right = 3, cex.axis = 1,
```

4 Descriptive and statistical summaries

cex.legend = c(1.2, 1.2), legend = c(TRUE, FALSE))

Descriptive statistics for copy number and genotype calls are provided with the summary method. For each chromosome in the AnnotatedSnpSet, summary calculates the average and standard deviation of the copy number estimates, as well as the % homozygous and heterozygous calls. In addition, summary calculates the average copy number, standard deviation, % homozygous and heterozygous across all autosomes in the AnnotatedSnpSet. The dimensions of the four matrices are S x C + 1, where S is the number of samples and C is the number of chromosomes in the AnnotatedSnpSet.

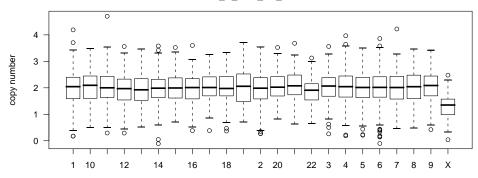
```
> x <- summary(annSnpset, digits = 1)
> str(x)

List of 5
$ avgCN : num [1:6, 1:23] 2 2 2 2 2 2 2 2 2 2 2 2 2 ...
..- attr(*, "dimnames")=List of 2
....$ : chr [1:6] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
....$ : chr [1:23] "1" "2" "3" "4" ...
```

```
..- attr(*, "dimnames")=List of 2
 ....$: chr [1:6] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
   ..$ : chr [1:23] "1" "2" "3" "4" ...
$ %NoCalls: num [1:6, 1:23] 0 0 0 0 0 0 0 0 0 0 ...
 ..- attr(*, "dimnames")=List of 2
 ....$: chr [1:6] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
 ....$: chr [1:23] "1" "2" "3" "4" ...
$ %Hom
         ..- attr(*, "dimnames")=List of 2
 ....$ : chr [1:6] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
    ..$ : chr [1:23] "1" "2" "3" "4" ...
$ %Het
         : num [1:6, 1:23] 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 0.3 ...
 ..- attr(*, "dimnames")=List of 2
 ....$: chr [1:6] "NA17101_X_hAF_A1_4000091.CEL" "NA17102_X_hAF_A2_4000091.CEL" "NA17103_X_hAF_A3_4
 .. ..$ : chr [1:23] "1" "2" "3" "4" ...
Boxplot by chromosome:
> par(mfrow = c(1, 1), mar = c(4, 4, 3, 1), las = 1)
```

- > boxplot(split(copyNumber(annSnpset[, 1]), chromosome(annSnpset)),
- ylab = "copy number", main = sampleNames(annSnpset)[1])

NA17101_X_hAF_A1_4000091.CEL



Smoothing example

\$ sdCN

The basic unit for all of the above visualization tools and summary methods is an AnnotatedSnpSet of a single chromosome. For instance, plotSnp converts the AnnotatedSnpSet to a list of AnnotatedSnpSet, where each element in the list is an AnnotatedSnpSet of a single chromosome. In the code below, we are interested in a quick method for smoothing copy number estimates for each chromosome and apply a loess smoother to each chromosome. The following code chunk first assigns heterozygous calls to the integer 1 and homozygous calls to the integer zero. In this way, regions of deletions will have homozygous calls of zero. We simulated a deletion of 50 consecutive SNPs and then converted the AnnotatedSnpSet to a list where each element in the list is an AnnotatedSnpSet for a particular chromosome.

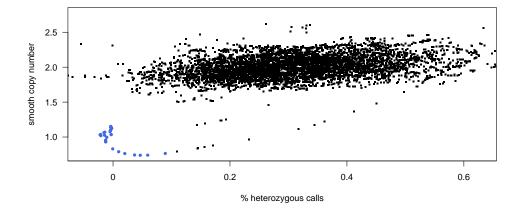
```
> sim1 <- annSnpset[chromosome(annSnpset) %in% 1:5, 1:3]
> sim1
```

AnnotatedSnpSet (storageMode: lockedEnvironment) assayData: 2212 features, 3 samples

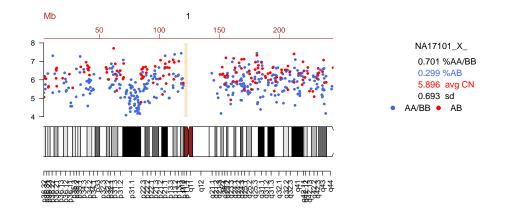
```
element names: calls, callsConfidence, cnConfidence, copyNumber
phenoData
An object of class "AnnotatedDataFrame"
  sampleNames: NA17101_X_hAF_A1_4000091.CEL, NA17102_X_hAF_A2_4000091
  .CEL, NA17103_X_hAF_A3_4000091.CEL
  varLabels and varMetadata description: none
featureData
An object of class "AnnotatedDataFrame"
  rowNames: SNP_A-1507972, SNP_A-1641781, ..., SNP_A-1759046 (2212 total)
  varLabels and varMetadata description:
    dbsnp_rs_id: dbsnp_rs_id
    chrom: chrom
    ...: ...
    enzyme: enzyme
    (8 total)
experimentData: use 'experimentData(object)'
Annotation [1] "pd.mapping50k.xba240"
chromosomeAnnotation
   centromereStart centromereEnd chromosomeSize
         121147476 123387476
                                       245522847
1
2
          91748045
                        94748045
                                       243018229
3
          90587544
                        93487544
                                      199505740
4
          49501045
                        52501045
                                      191411218
5
          46441398
                        49441398
                                      180857866
6
          58938125
                        61938125
                                      170975699
7
          57864988
                        60864988
                                       158628139
8
                        46958052
          43958052
                                      146274826
9
          46035928
                        49035928
                                      138429268
10
          39244941
                        41624941
                                      135413628
11
          51450781
                        54450781
                                      134452384
12
          34747961
                        36142961
                                      132449811
13
          16000000
                        17868000
                                      114142980
14
          15070000
                        18070000
                                      106368585
15
          15260000
                        18260000
                                       100338915
16
          35143302
                        36943302
                                        88827254
17
          22187133
                        22287133
                                       78774742
18
          15400898
                        16764896
                                       76117153
19
          26923622
                        29923622
                                        63811651
20
                        28033230
                                        62435964
          26267569
21
          10260000
                        13260000
                                       46944323
22
          11330000
                        14330000
                                       49554710
Х
          58465033
                        61465033
                                      154824264
γ
          11237315
                        12237315
                                       57701691
> tmp <- sim1[chromosome(sim1) == "1", ]</pre>
> tmp <- tmp[order(position(tmp)), ]</pre>
> snps <- featureNames(tmp)[101:150]</pre>
> ids <- match(snps, featureNames(sim1))</pre>
> copyNumber(sim1)[ids, 1] <- copyNumber(sim1)[ids, 1] -</pre>
      1
```

```
> calls(sim1)[ids, 1] <- 1
> sim2 <- sim1
> calls(sim2)[calls(sim2) == 1 | calls(sim2) == 3] <- 0
> calls(sim2)[calls(sim2) == 2] <- 1
> sim.list <- split(sim2, chromosome(sim2))</pre>
> sim.list[[1]]
AnnotatedSnpSet (storageMode: lockedEnvironment)
assayData: 469 features, 3 samples
  element names: calls, callsConfidence, cnConfidence, copyNumber
phenoData
An object of class "AnnotatedDataFrame"
  sampleNames: NA17101_X_hAF_A1_4000091.CEL, NA17102_X_hAF_A2_4000091
  .CEL, NA17103_X_hAF_A3_4000091.CEL
  varLabels and varMetadata description: none
featureData
An object of class "AnnotatedDataFrame"
 rowNames: SNP_A-1642387, SNP_A-1643189, ..., SNP_A-1759036 (469 total)
 varLabels and varMetadata description:
   dbsnp_rs_id: dbsnp_rs_id
   chrom: chrom
    ...: ...
   enzyme: enzyme
    (8 total)
experimentData: use 'experimentData(object)'
Annotation [1] "pd.mapping50k.xba240"
chromosomeAnnotation
  centromereStart centromereEnd chromosomeSize
1
        121147476 123387476
                                     245522847
2
         91748045
                      94748045
                                     243018229
3
         90587544
                       93487544
                                     199505740
4
         49501045
                       52501045
                                     191411218
5
         46441398
                       49441398
                                     180857866
6
         58938125
                      61938125
                                     170975699
7
         57864988
                      60864988
                                     158628139
8
         43958052
                      46958052
                                     146274826
9
         46035928
                      49035928
                                     138429268
10
         39244941
                       41624941
                                     135413628
11
         51450781
                       54450781
                                     134452384
12
         34747961
                       36142961
                                     132449811
13
         16000000
                       17868000
                                     114142980
14
                       18070000
         15070000
                                     106368585
15
         15260000
                       18260000
                                     100338915
16
         35143302
                       36943302
                                      88827254
17
         22187133
                       22287133
                                      78774742
18
                                      76117153
         15400898
                       16764896
19
         26923622
                       29923622
                                      63811651
20
         26267569
                       28033230
                                      62435964
21
         10260000
                       13260000
                                      46944323
22
         11330000
                       14330000
                                      49554710
```

```
X
          58465033
                         61465033
                                         154824264
Y
          11237315
                         12237315
                                          57701691
> smoothChromosome <- function(obj, span) {</pre>
      loessX <- function(X, location, span) {</pre>
+
           fit <- loess(X ~ location, span = span)$fitted
+
          return(fit)
      }
      obj <- obj[order(position(obj)), ]</pre>
      cn.smooth <- apply(copyNumber(obj), 2, loessX, position(obj),</pre>
          span = span)
      rownames(cn.smooth) <- featureNames(obj)</pre>
      call.smooth <- apply(calls(obj), 2, loessX, location = position(obj),</pre>
           span = span)
      rownames(call.smooth) <- featureNames(obj)</pre>
+
      copyNumber(obj) <- cn.smooth</pre>
+
      calls(obj) <- call.smooth
      obj
+ }
> smoothList <- lapply(sim.list, smoothChromosome, span = 1/10)
> smoothSet <- unsplitS4(smoothList, featureData(sim2))</pre>
Or equivalently,
> smoothSet2 <- smoothSnp(sim1, 1:5, 1:3, span = 1/10)
> identical(copyNumber(smoothSet2), copyNumber(smoothSet))
[1] TRUE
> identical(calls(smoothSet2), calls(smoothSet))
[1] TRUE
A plot of the smoothed calls versus copynumber can be used to visualize the deletion and deciding on
a threshold for calling deletions.
> par(las = 1, mar = c(5, 4, 0.5, 0.5), oma = rep(0, 4))
> plot(calls(smoothSet2), copyNumber(smoothSet2), ylim = range(copyNumber(smoothSet2)),
      pch = ".", cex = 3, xlab = "% heterozygous calls",
      ylab = "smooth copy number", xaxt = "n", xlim = c(-0.05,
          30/70 + 0.2))
> axis(1, at = pretty(calls(smoothSet2)), labels = pretty(calls(smoothSet2)))
> highlight <- calls(smoothSet2) <= 0.1 & copyNumber(smoothSet2) <=</pre>
      1.5
> points(calls(smoothSet2)[highlight], copyNumber(smoothSet2)[highlight],
      pch = 20, col = "royalblue", bg = "white")
```



```
> copyNumber(sim1) <- copyNumber(sim1) + 2
> plotSnp(sim1, 1, 1, log = "", width.right = 0.5, cex.legend = c(1.2,
+ 1.2), legend.panel = c(TRUE, FALSE), cex = c(1,
+ 1, 1), pch = rep(20, 3), legend.location = c("topright",
+ "bottomright"), addCytoband = TRUE)
```



5 Integration with other Bioconductor packages

To retreive additional annotation on the known SNP's in the region of this simulated deletion, we could use the RSNPper. The installation instructions for RSNPper is available at Bioconductor.

```
> library(RSNPper)
> (dbId <- dbSnpId(annSnpset)[snps[2] == featureNames(annSnpset)])
> dbId <- strsplit(dbId, "rs")[[1]][2]
> print(SNPinfo(dbId))
```

6 Session Information

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

• R version 2.6.0 Under development (unstable) (2007-07-08 r42150), powerpc-apple-darwin8.10.0

- Locale: C
- Base packages: base, datasets, grDevices, graphics, methods, splines, stats, tools, utils
- Other packages: AnnotationDbi 0.0.77, Biobase 1.15.19, BufferedMatrix 1.1.0, BufferedMatrixMethods 1.1.0, DBI 0.2-3, RSQLite 0.5-4, SNPchip 1.1.9, affyio 1.5.0, annotate 1.15.1, geneplotter 1.15.1, lattice 0.15-8, oligo 1.1.5, preprocessCore 0.99.8
- Loaded via a namespace (and not attached): KernSmooth 2.22-20, RColorBrewer 0.2-3, grid 2.6.0