Using the DNaseI hypersensitivity data from encode in R

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1 Introduction

Annotation tracks from UCSC hg18 can be used with Bioconductor to help establish genomic contexts of events or alterations. The CD4-based hypersensitivity assays are collected in the structure rawCD4 in package encoDnaseI:

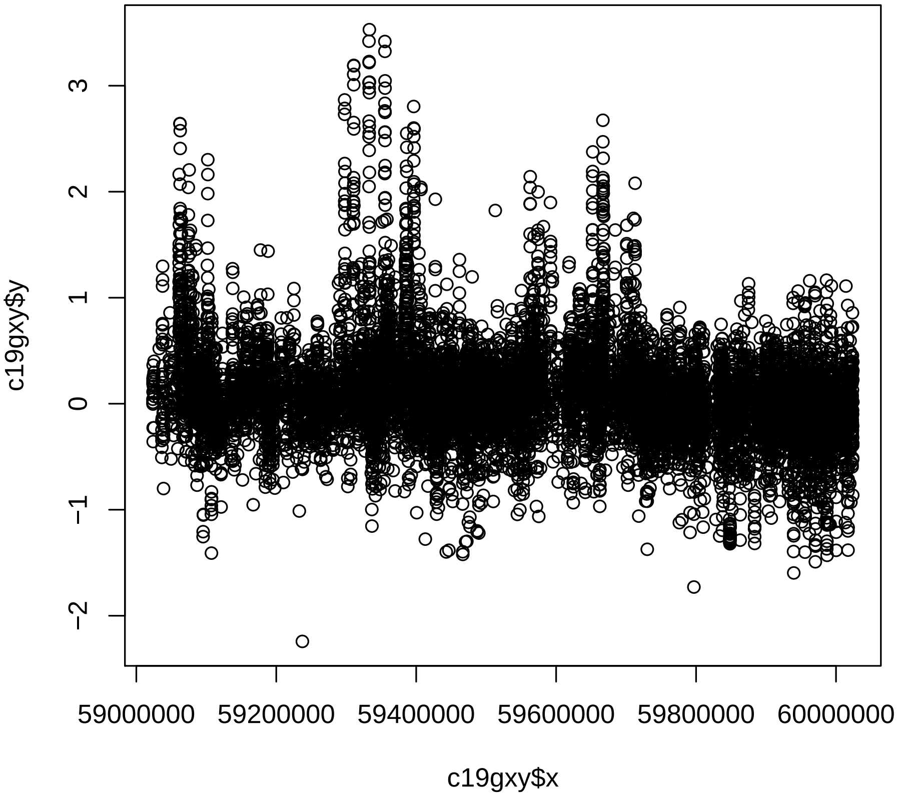
```
> library(encoDnaseI)

Loading package ff 2.1-2
- getOption("fftempdir")=="E:/biocbld/bbs-2.6-data-experiment/tmpdir/RtmpaIdYXw"
- getOption("ffextension")=="ff"
- getOption("ffdrop")==TRUE
- getOption("fffinonexit")==TRUE
- getOption("ffpagesize")==65536
- getOption("ffcaching")=="mmnoflush"  -- consider "ffeachflush" if your system stalls
- getOption("ffbatchbytes")==16095641 -- consider a different value for tuning your sys
Attaching package ff

> data(rawCD4)
> rawCD4

hg18track (storageMode: lockedEnvironment)
assayData: 382713 features, 1 samples
  element names: dataVals
protocolData: none
phenoData: none
featureData
  featureNames: 1, 2, ..., 382713  (382713 total)
  fvarLabels and fvarMetadata description:
    bin: given bin
    chrom: chr..
    chromStart: numeric origin
    chromEnd: numeric close
experimentData: use 'experimentData(object)'
  pubMedIds: 16791207
Annotation:
```

At present, we can subset the data by casting a chromosome number:

```
> c19g = rawCD4[chrnum(19)]
> c19g

hg18track (storageMode: lockedEnvironment)
assayData: 11158 features, 1 samples
  element names: dataVals
protocolData: none
phenoData: none
featureData
  featureNames: 129572, 129573, ..., 140729  (11158 total)
  fvarLabels and fvarMetadata description:
    bin: given bin
    chrom: chr..
    chromStart: numeric origin
    chromEnd: numeric close
experimentData: use 'experimentData(object)'
  pubMedIds: 16791207
Annotation:
```

And we can get a trace of values along the chromosome:

```
> c19gxy = getTrkXY(c19g)
> plot(c19gxy)
```



2 Coupling the DnaseI series to genetics of gene expression

We would like to subset a racExSet from GGdata and look at snps that are in regions of high DNaseI sensitivity. Some infrastructure to help with this is:

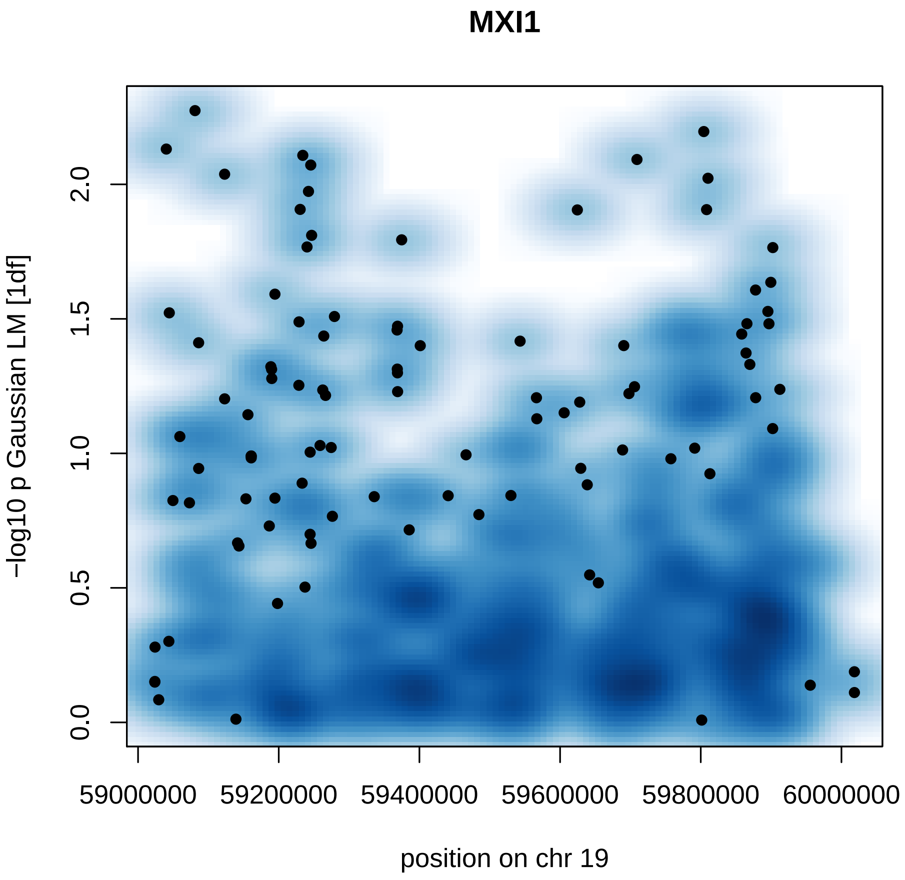
```
> clipSnps = function(sms, chrn, lo, hi) {
+     allp = getSnpLocs(sms)
+     allp = allp - allp[1]
+     ok = allp >= lo & allp <= hi
+     thesm = smList(sms)[[1]]
+     rsn = colnames(thesm)
+     rid = rsn[which(ok)]
+     thesm = thesm[, rid, drop = FALSE]
+     nn = new.env()
+     tmp = list(thesm)
+     names(tmp) = as.character(chrn)
+     assign("smList", tmp, nn)
+     sms@smlEnv = nn
+     sms@activeSnpInds = which(ok)
+     sms
+ }
> rangeX = function(htrk) {
+     range(getTrkXY(htrk)$x)
+ }
```

So we get the information on expression and SNPs in chr19g and filter:

```
> library(GGtools)
> library(GGdata)
> if (!exists("hmceuB36")) data(hmceuB36)
> rs19g = rangeX(c19g)
> h19 = hmceuB36[chrnum(19), ]
> h19locs = getSnpLocs(hmceuB36[chrnum(19), ])[[1]]
> goodlocs = which(h19locs[2, ] >= rs19g[1] & h19locs[2, ] <= rs19g[2])
> h19rsn = paste("rs", h19locs[1, goodlocs], sep = "")
> h19trim = h19[rsid(h19rsn), ]
```

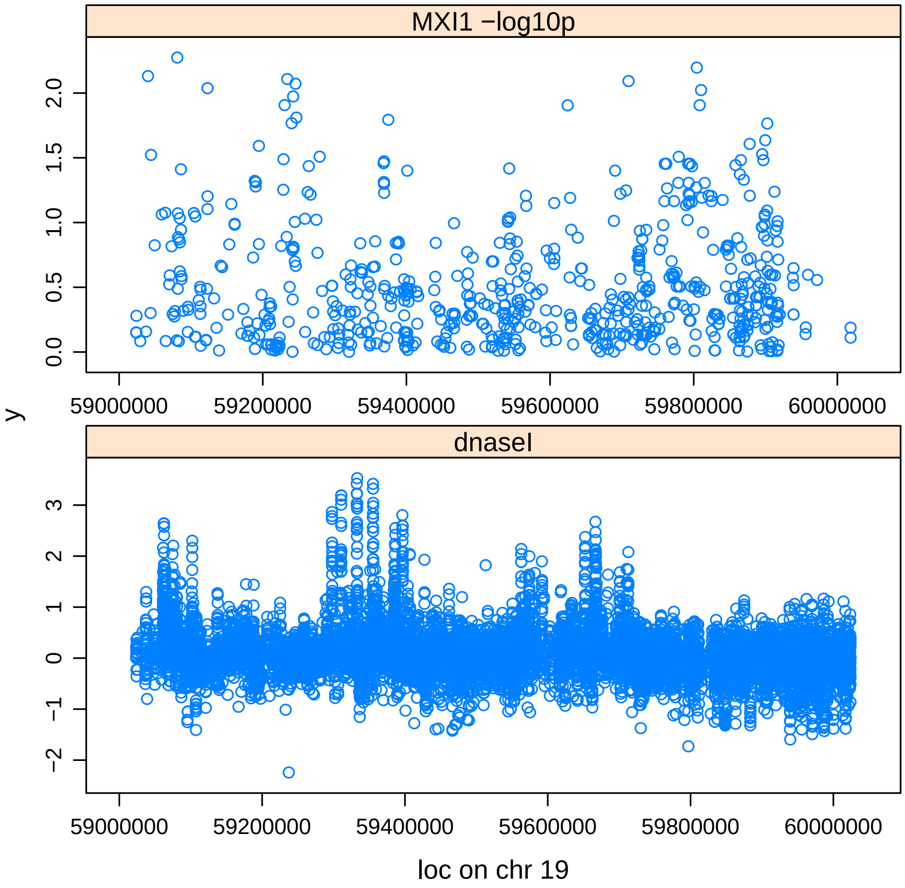
A gene-specific screen can be computed as follows:

```
> oo = options()
> options(warn = 0)
> library(GGtools)
> showMethods("gwSnpTests")

Function: gwSnpTests (package GGtools)
sym="formula", sms="smlSet", cnum="cnumOrMissing", cs="missing"
sym="formula", sms="smlSet", cnum="snpdepth", cs="chunksize"
sym="formula", sms="smlSet", cnum="snpdepth", cs="missing"

> smxi1 = gwSnpTests(genesym("MXI1") ~ 1 - 1, h19trim, chrnum(19))

[1] "GI_18641367-A" "GI_18641367-I" "GI_18641369-I"

> plot(smxi1)
> options(oo)
```



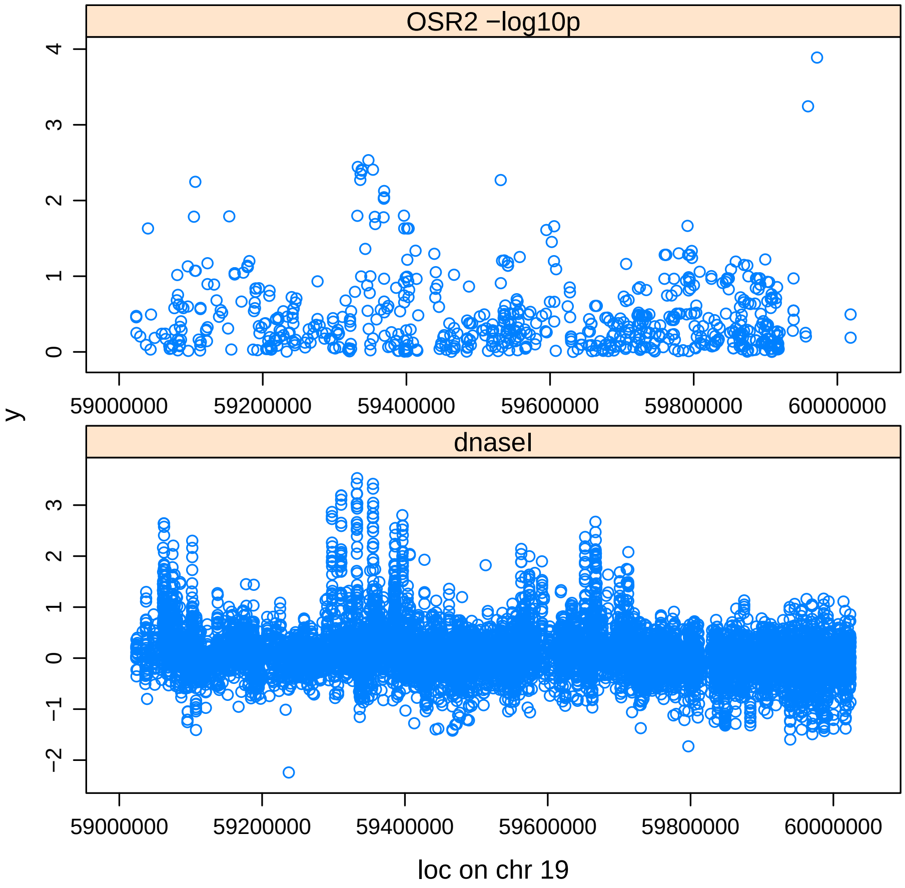
We'd like to look at the SNP screen results juxtaposed with the DnaseI results.

```
> print(juxtaPlot(c19g, smxi1))
```



Another example:

```
> oo = options()
> options(warn = 0)
> sOSR2 = gwSnpTests(genesym("OSR2") ~ 1 - 1, h19trim, chrnum(19))
> print(juxtaPlot(c19g, sOSR2))
> options(oo)
```



We can score the highly associated snps for closeness to a highly DnaseI sensitive region using ALICOR:

```
> ALICOR(sOSR2, c19g)

[1] 0.2678520

> ALICOR(smxi1, c19g)

[1] -0.01268991

> if (interactive()) {
+     if (!exists("mads"))
+         mads = apply(exprs(c19gf), 1, mad)
+     if (interactive())
+         fn = featureNames(c19gf)[which(mads > quantile(mads,
+             0.6))]
+     if (!interactive())
+         fn = featureNames(c19gf)[which(mads > quantile(mads,
+             0.97))]
+     n19g = c19gf[exFeatID(fn), ]
+     if (file.exists("tw19g.rda"))
+         load("tw19g.rda")
+     if (!exists("tw19g"))
+         tw19g = twSnpScreen(n19g, chr19gmeta, ~., fastAGMfitter)
+     if (!file.exists("tw19g.rda"))
+         save(tw19g, file = "tw19g.rda")
+     if (file.exists("allscor.rda"))
+         load("allscor.rda")
+     if (!exists("allscor"))
+         allscor = sapply(tw19g, function(x) {
+             if (inherits(x, "try-error"))
+                 return(NA)
+             else return(ALICOR(x, c19g))
+         })
+     if (!file.exists("allscor.rda"))
+         save(allscor, file = "allscor.rda")
+ }
```

With these scores, we can find gene-snp combinations for which association is at least partly synchronized with DHS. Algorithms for systematically assessing synchronicity are in development.