Prototype QTL Strategy: Phenotype bp in Cross hyper

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Automated Strategy

- Estimate positions and effects of main QTL.
- Find chromosomes with epistasis.
- Estimate epistatic pair positions and effects.
- Confirm genetic architecture with ANOVA.

Running Sweave

```
> library(qtlbim)

> qb.sweave(hyper, pheno.col = 1,
+  n.iter = 3000, n.draws = 8,
+  scan.type = "2logBF", hpd.level = 0.5,
+  threshold = c(upper = 2),
+  SweaveFile = "/tmp/Rinst373444505/qtlbim/doc/hyperslide.Rnw",
+  SweaveExtra = "/tmp/Rinst373444505/qtlbim/external/hyperslideextra.Rnw",
+  PDFDir = "bpPDF",
+  remove.qb = TRUE)
```

Cross Object

```
> summary(cross)

    Backcross

    No. individuals:    250

    No. phenotypes:     2
    Percent phenotyped: 100 100

    No. chromosomes:    19
        Autosomes:      1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

    Total markers:      170
    No. markers:        22 8 6 20 14 11 7 6 5 5 14 5 5 5 11 6 12 4 4
    Percent genotyped:  47.9
    Genotypes (%):      AA:50.1  AB:49.9
```

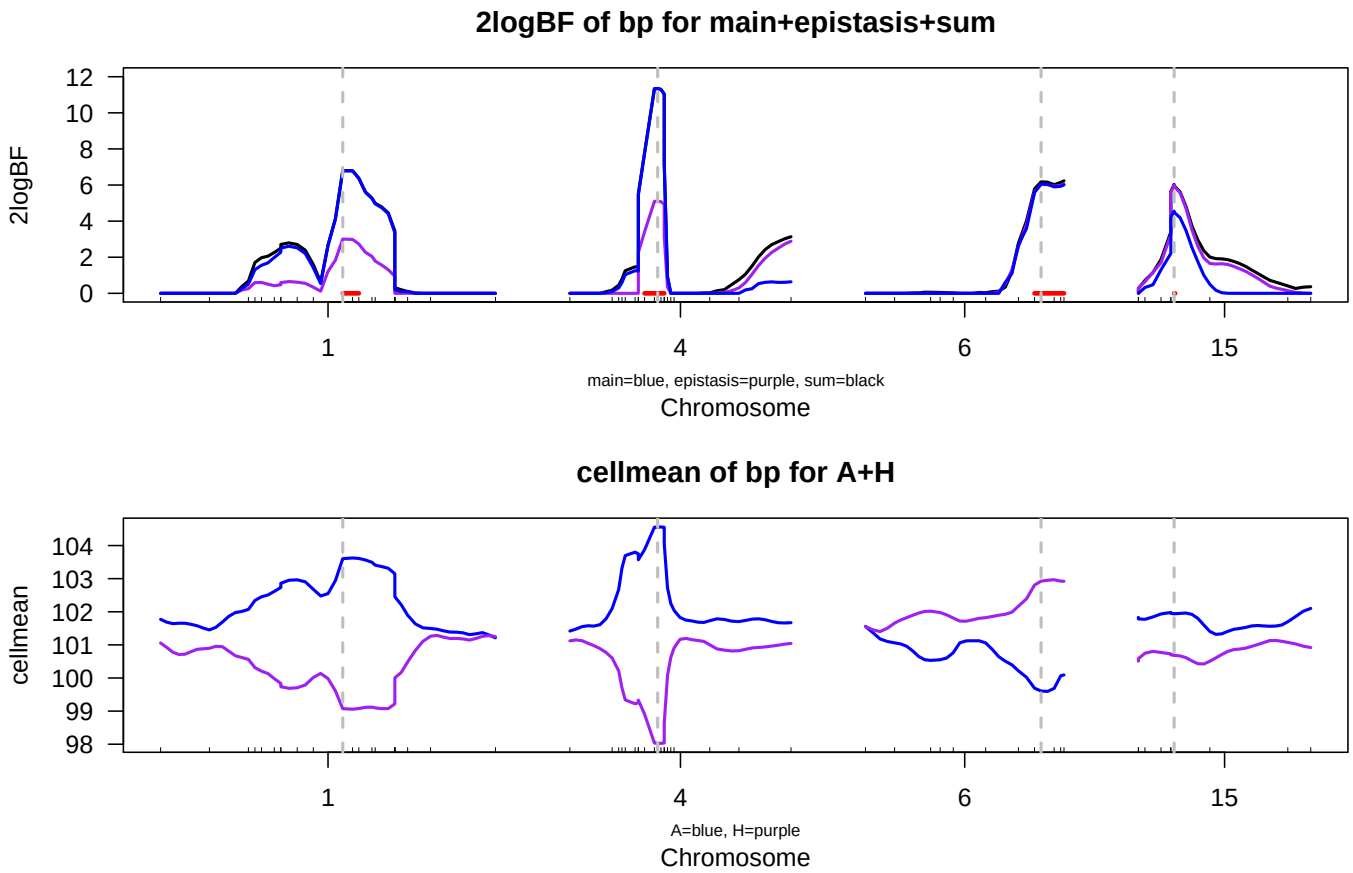
Create MCMC runs

```
> cross <- qb.genoprob(cross,step=2)
> cross.qb <- qb.mcmc(cross, pheno.col = pheno.col,
+   genoupdate=TRUE, n.iter = 3000, verbose=FALSE)
```

1-D 2logBF Scan

```
> hpd.level

[1] 0.5

> cross.hpd <- qb.hpdone(cross.qb, hpd.level)
> sum.one <- summary(cross.hpd)
> sum.one

   chr n.qtl  pos lo.50% hi.50% 2logBF       A       H
1    1 0.694 64.5   64.5   69.9  6.796 103.604  99.073
4    4 3.460 29.5   25.1   31.7 11.347 104.561  98.026
6    6 1.107 59.0   56.8   66.7  6.179  99.606 102.924
15  15 0.341 17.5   17.5   17.5  6.032 101.940 100.692

> chrs <- as.vector(sum.one[, "chr"])
> pos <- sum.one[, "pos"]

> plot(cross.hpd, profile = scan.type)
```

1-D Scan: 2logBF Profile



2-D: find epistatic pairs

```
> two <- qb.scantwo(cross.qb, chr = chrs, type = scan.type)
> sum.two <- summary(two, sort = "upper", threshold = threshold,
+     refine = TRUE)
> sum.two

upper: 2logBF of bp for epistasis
lower: 2logBF of bp for full
Thresholds: upper=2

        n.qtl l.pos1 l.pos2 lower u.pos1 u.pos2 upper
c6 :c15 1.080   59.0   17.5 12.78   59.0   17.5 12.75
c4 :c6  1.561   29.5   66.7 14.88   74.3   59.0  7.73
c4 :c15 0.446   29.5   17.5 14.54   74.3   35.5  7.35
c1 :c4  1.352   67.8   29.5 15.71   72.1   29.5  7.30
c15:c15 0.105   17.5   27.5  8.13   17.5   25.5  7.23
c1 :c15 1.145   67.8   17.5 12.01   77.6   17.5  5.79
c1 :c6  1.831   67.8   59.0 12.61   75.4   65.6  4.76
c4 :c4  0.298   29.5   74.3 11.82    0.0   28.4  4.76
c6 :c6  1.214   61.2   65.6  7.44   27.3   65.6  4.76
c1 :c1  0.362   46.5   75.4  7.61   43.7   74.3  4.70
```

Initial Genetic Architecture

```
> cross.arch <- qb.arch(sum.two, chrs, pos)
> cross.arch

main QTL loci:
       1     2 3     4    5    6     7    8     9
chr  1.0  1.00 4  4.00  4.0  6.0  6.00 15.0 15.00
pos 43.7 72.78 0 29.13 74.3 27.3 61.64 19.1 35.55

Epistatic pairs by qtl, chr, pos:
  qtla qtlb chra chrb  posa  posb
1    7    8    6   15 61.64 19.10
2    5    7    4    6 74.30 61.64
3    5    9    4   15 74.30 35.55
4    2    4    1    4 72.78 29.13
5    2    8    1   15 72.78 19.10
6    2    7    1    6 72.78 61.64
7    3    4    4    4  0.00 29.13
8    6    7    6    6 27.30 61.64
9    1    2    1    1 43.70 72.78
Epistatic chromosomes by connected sets:
1,4,6,15
```

Construct QTL Object

use R/qtl tools to check model fit
first simulate missing markers
then construct QTL object

```
> cross.sub <- subset(cross, chr = cross.arch$qtl$chr)
> n.draws

[1] 8

> cross.sub <- sim.geno(cross.sub, n.draws = n.draws, step = 2,
+     error = 0.01)
> qtl <- makeqtl(cross.sub, cross.arch$qtl$chr, cross.arch$qtl$pos)
> cross.sub <- clean(cross.sub)
```

Stepwise Reduction

```
> cross.step <- step.fitqtl(cross.sub, qtl, pheno.col, cross.arch)

  drop                    LOD     p
1 Chr6@27.3:Chr6@61.64  -0.3290 1.0000
2 Chr1@72.78:Chr6@61.64  0.0237 0.7500
3 Chr4@0:Chr4@29.13      0.1200 0.4730
4 Chr4@0                -0.0255 1.0000
5 Chr1@72.78:Chr15@19.1  0.1670 0.3960
6 Chr4@74.3:Chr6@61.64   0.6630 0.0899
7 Chr1@43.7:Chr1@72.78   0.8230 0.0583

> summary(cross.step$fit)

       df         SS        MS      LOD     %var Pvalue(Chi2) Pvalue(F)
Model  11  7354.765 668.61496 29.22201 41.62540            0         0
Error 238 10314.172  43.33686
Total 249 17668.936
```

Stepwise Reduction

	df	Type III SS	LOD	%var	F value	Pvalue(F)	
Chr1@43.7	1	365.3747	1.8898	2.0679	8.431	0.00404	**
Chr1@72.78	2	561.6735	2.8786	3.1789	6.480	0.00182	**
Chr4@29.13	2	2376.4769	11.2562	13.4500	27.419	1.92e-11	***
Chr4@74.3	2	956.3169	4.8135	5.4124	11.034	2.62e-05	***
Chr6@27.3	1	247.1278	1.2854	1.3987	5.702	0.01772	*
Chr6@61.64	2	1847.7821	8.9461	10.4578	21.319	3.04e-09	***
Chr15@19.1	2	1822.1058	8.8314	10.3125	21.023	3.91e-09	***
Chr15@35.55	2	850.2809	4.3004	4.8123	9.810	8.05e-05	***
Chr6@61.64:Chr15@19.1	1	1561.6654	7.6537	8.8385	36.036	7.18e-09	***
Chr4@74.3:Chr15@35.55	1	824.4493	4.1746	4.6661	19.024	1.92e-05	***
Chr1@72.78:Chr4@29.13	1	171.0187	0.8927	0.9679	3.946	0.04812	*

Reduced Genetic architecture

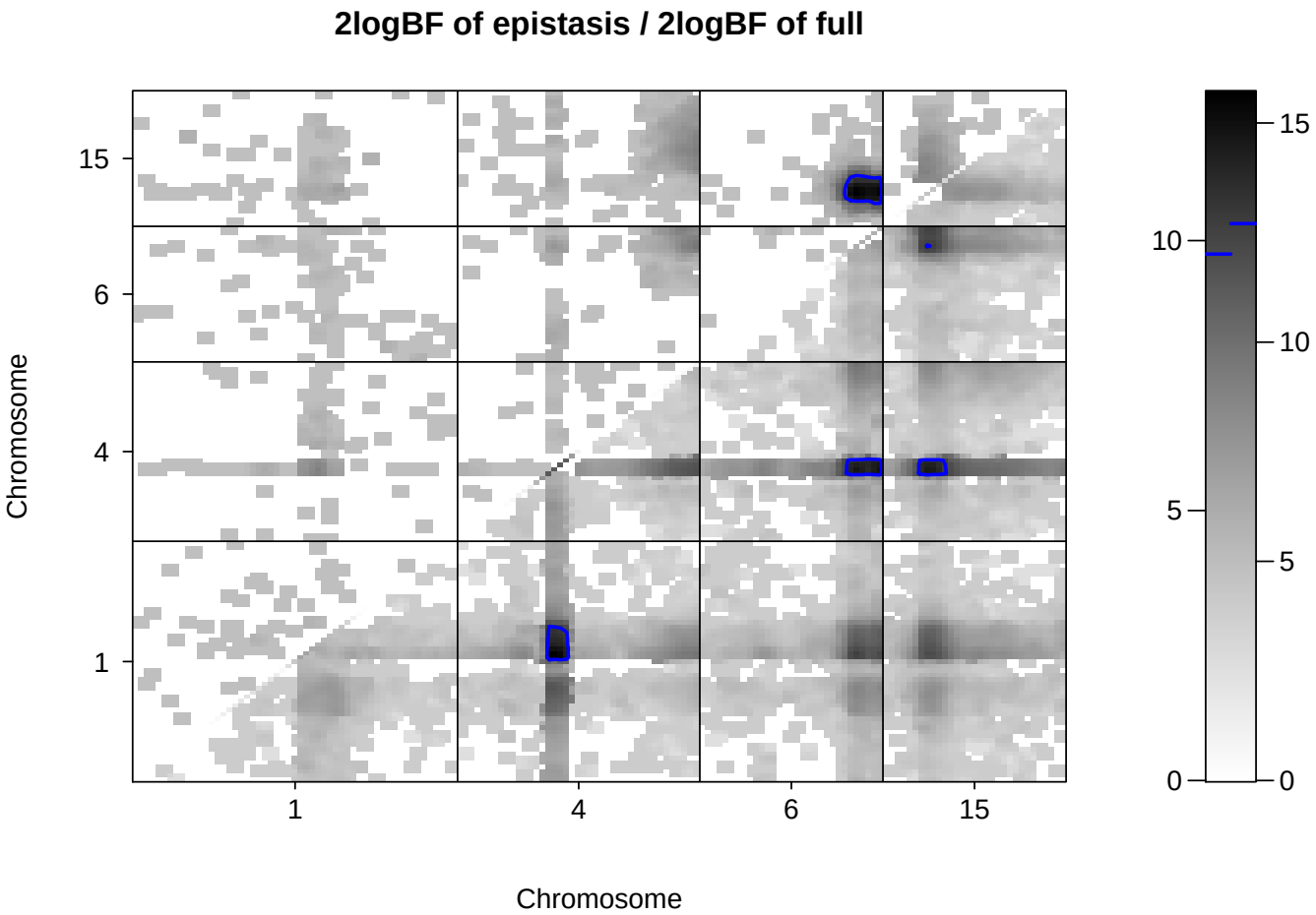
```
> cross.arch <- cross.step$arch
> cross.arch

main QTL loci:
       1     2     4    5    6     7    8     9
chr  1.0  1.00  4.00  4.0  6.0  6.00 15.0 15.00
pos 43.7 72.78 29.13 74.3 27.3 61.64 19.1 35.55

Epistatic pairs by qtl, chr, pos:
  q1 q2 chra chrb  posa  posb
1  7  8    6   15 61.64 19.10
2  5  9    4   15 74.30 35.55
3  2  4    1    4 72.78 29.13
Epistatic chromosomes by connected sets:
1,4,6,15
```

2-D Plots

2-D plots by cliques (if any epistasis)

```
> for(i in names(cross.arch$chr.by.set))
+   plot(two, chr = cross.arch$chr.by.set[[i]], smooth = 3,
+     col = "gray", contour = 3)
```

2-D Plots: clique 1

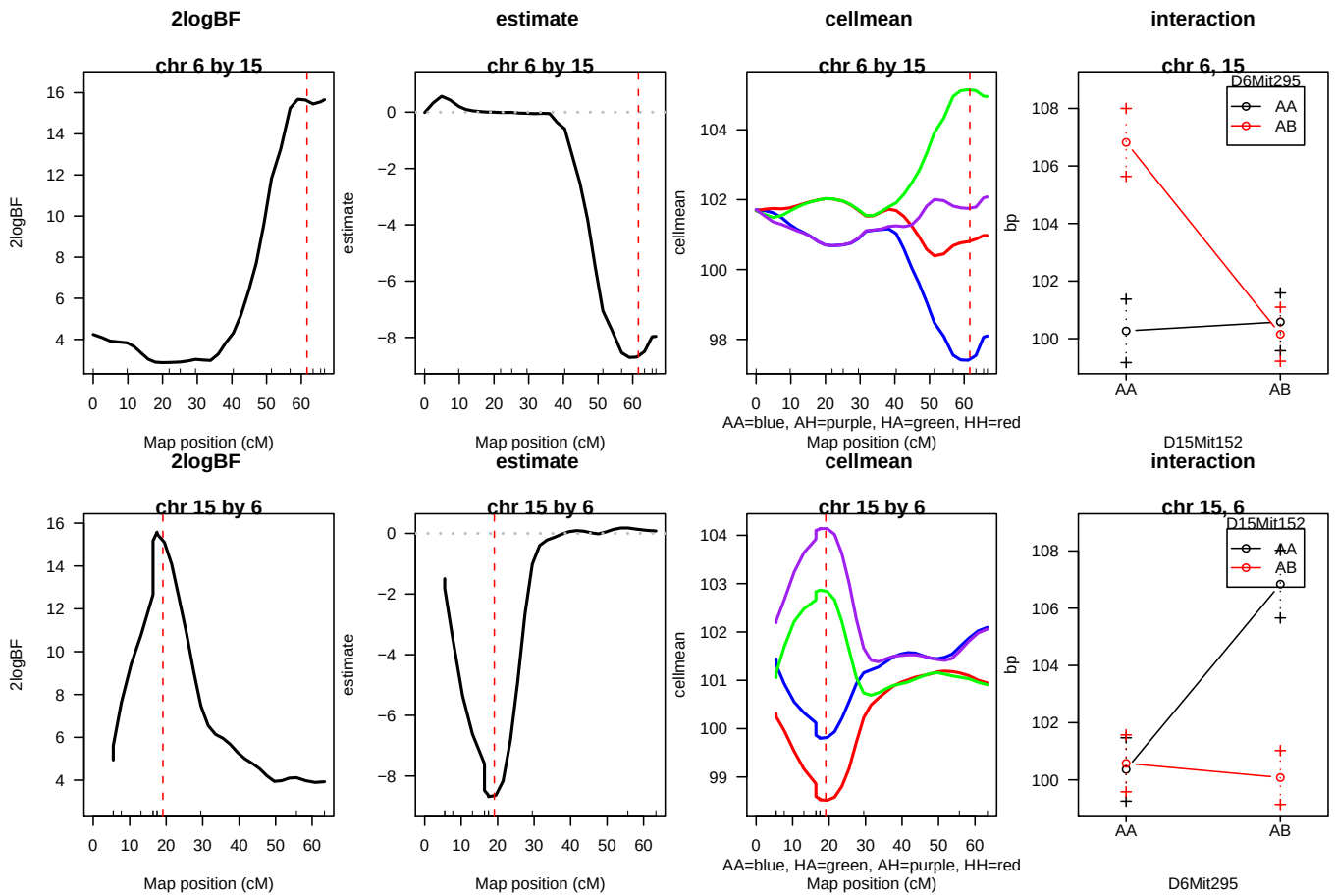


Slice Each Epistatic Pair

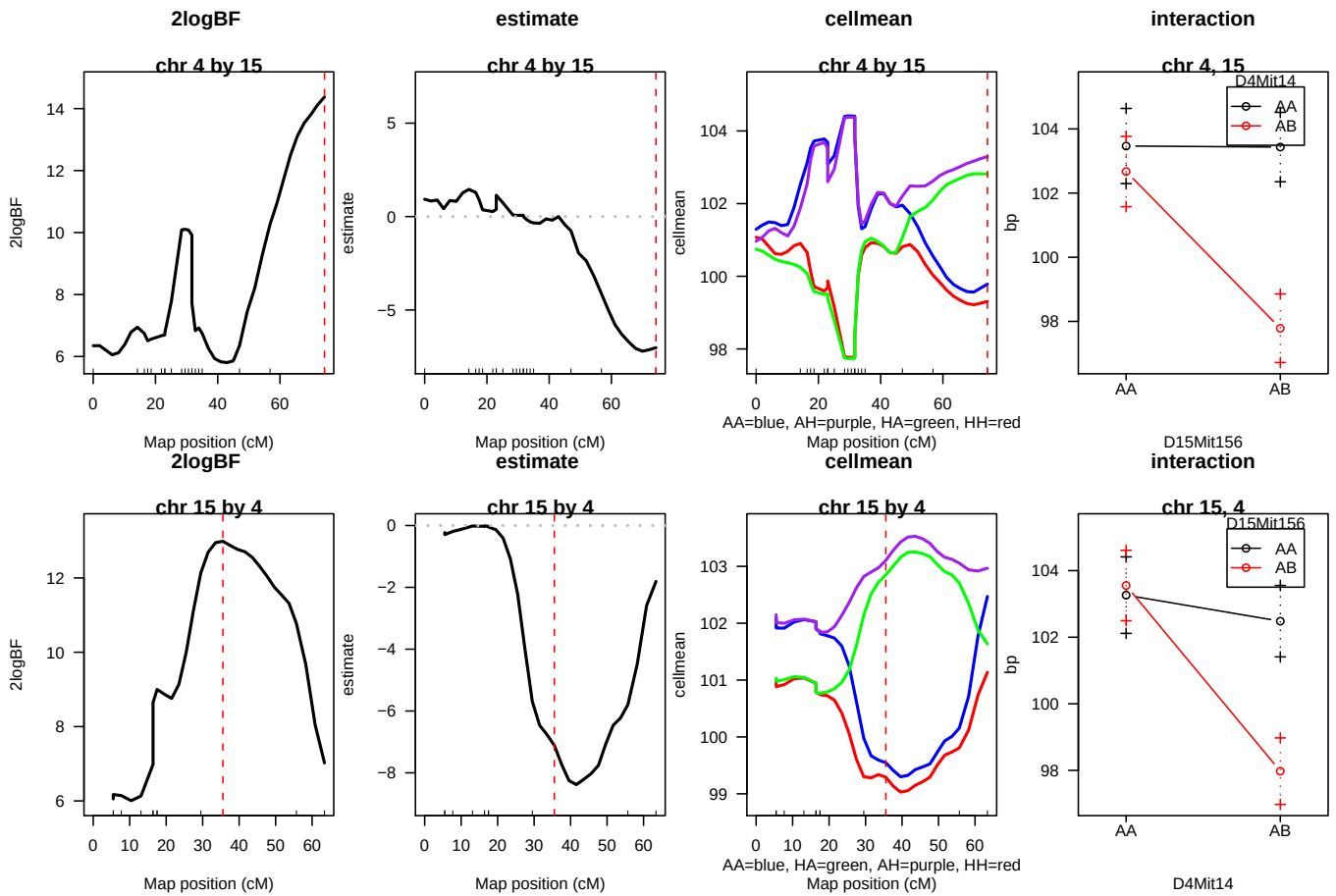
show detail plots for epistatic pairs (if any)

```
> if(!is.null(cross.arch$pair.by.chr)) {
+  for(i in seq(nrow(cross.arch$pair.by.chr$chr))) {
+    chri <- cross.arch$pair.by.chr$chr[i,]
+    posi <- cross.arch$pair.by.chr$pos[i,]
+    plot(qb.slicetwo(cross.qb, chri, posi, scan.type))
+  }
+}
```

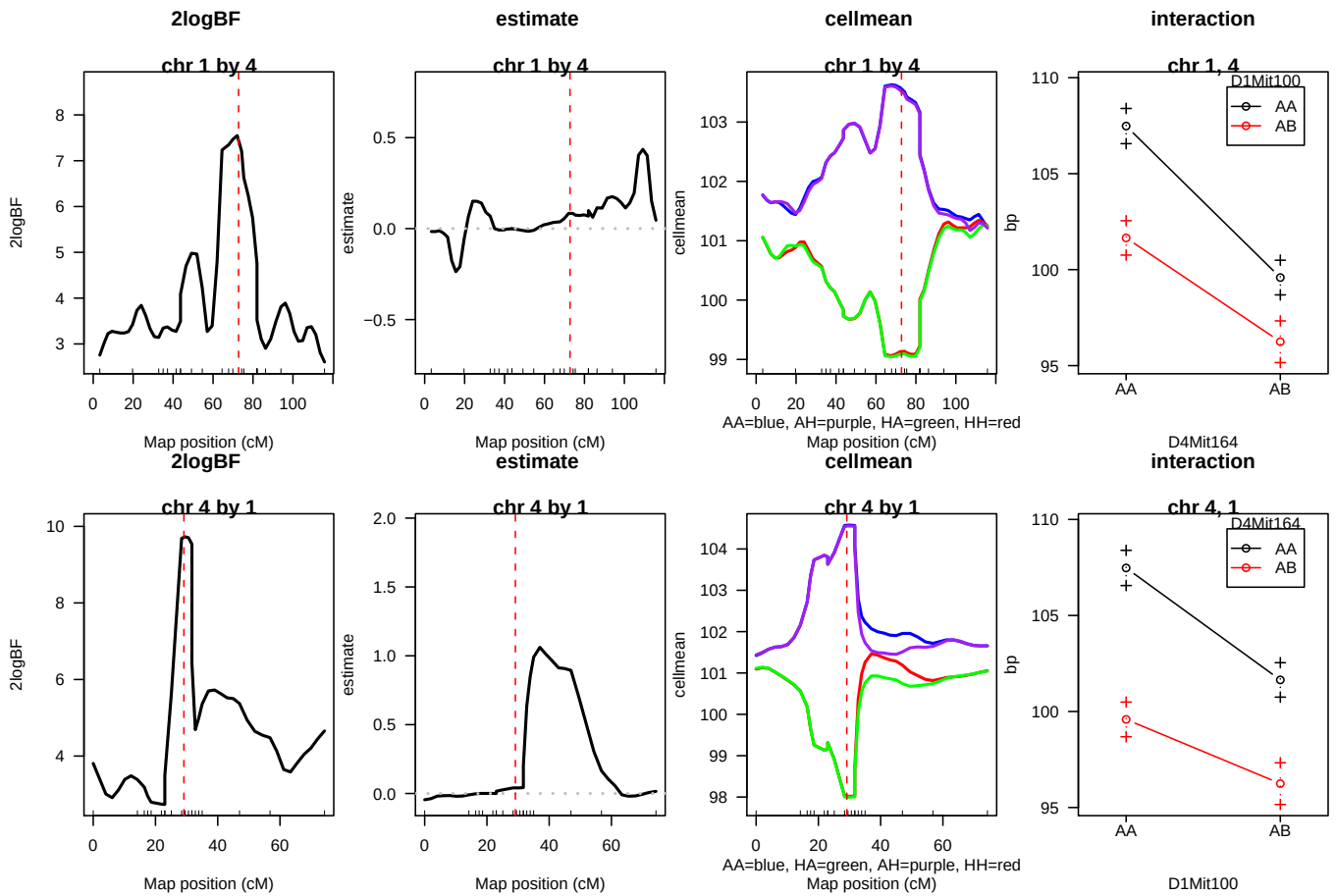
Epistatic Pair 6 and 15



Epistatic Pair 4 and 15



Epistatic Pair 1 and 4



Compare with Literature

Sugiyama et al. (2002) found:
two main QTLs on 1 4
two epistatic pairs with 6.15, 7.15
compare to present model:

```
> arch3 <- qb.arch(cross.step, main = c(1, 4), epistasis = data.frame(q1 = c(6,
+     7), q2 = rep(15, 2)))
> arch3
```

Sugiyama Model

```
> cross.step2 <- step.fitqtl(cross.sub, qtl, pheno.col, arch3)
> summary(cross.step2$fit)
```

Sugiyama vs. Automata

formal comparison with automated model

```
> anova(cross.step, cross.step2)
```

final tasks:
externally rename file hyperslide.tex to bp.tex
and run pdflatex twice on it
remove objects created by R/qtlbim if desired

```
> file.rename("hyperslide.tex", "bp.tex")
> invisible(system("pdflatex bp.tex",intern=TRUE))
> invisible(system("pdflatex bp.tex",intern=TRUE))

> remove.qb

[1] FALSE

> if (remove.qb) {
+     qb.remove(cross.qb)
+     rm(cross, cross.sub, pheno.col, threshold, n.iter, n.draws,
+         remove.qb)
+ }
```