Prototype QTL Strategy: Phenotype bp in Cross hyper

Brian S. Yandell, W. Whipple Neely, Nengjun Yi

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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 = 64,
+  scan.type = "2logBF", hpd.level = 0.5,
+  threshold = c(upper = 2),
+  SweaveFile = "/tmp/Rinst1519441970/qtlbim/doc/hyperslide.Rnw",
+  SweaveExtra = "/tmp/Rinst1519441970/qtlbim/external/hyperslideextra.Rnw",
+  PDFDir = "bpPDF",
+  remove.qb = TRUE)
```

Cross Object

```
> summary(cross)

    Backcross

    No. individuals:    250

    No. phenotypes:     1
    Percent phenotyped: 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
```

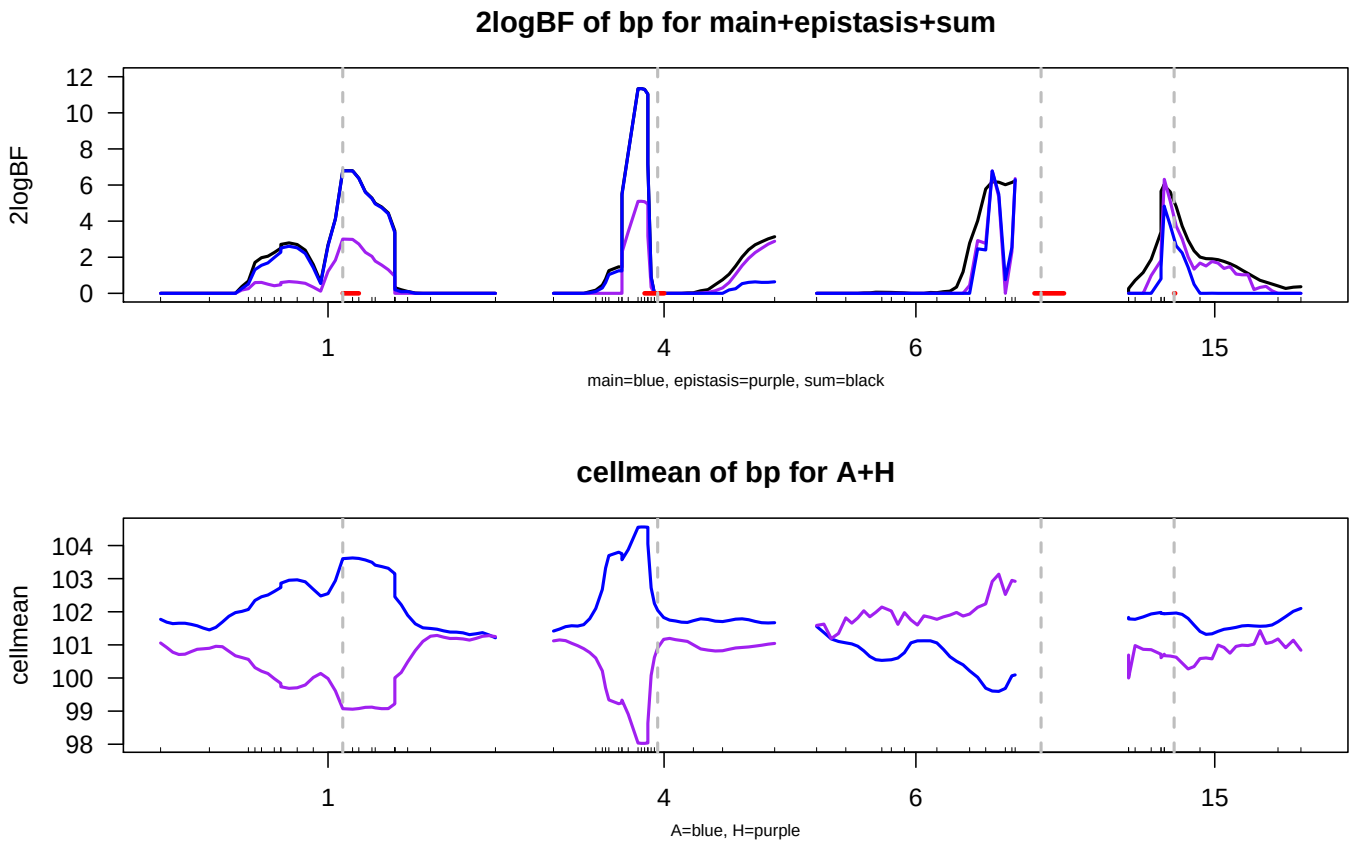
Create MCMC runs

```
> 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
<NA>   1 0.694 64.5   64.5   69.9  6.796 103.604  99.073
<NA>   4 3.460 29.5   25.1   31.7 11.347 104.561  98.026
<NA>   6 1.107 59.0   56.8   66.7  6.179  99.606 102.924
<NA>  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
```

	chr1	chr2	n.qtl	l.pos1	l.pos2	lower	u.pos1	u.pos2	upper
6:15	6	15	1.080	59.0	17.5	12.779	59.000	17.500	12.751
4:6	4	6	1.561	29.5	66.7	14.884	74.300	59.000	7.728
4:15	4	15	0.446	29.5	17.5	14.539	74.300	35.546	7.350
1:4	1	4	1.352	67.8	29.5	15.705	72.100	29.500	7.303
15:15	15	15	0.105	17.5	27.5	8.125	17.500	25.500	7.234
1:15	1	15	1.145	67.8	17.5	12.012	77.600	17.500	5.794
1:6	1	6	1.831	67.8	59.0	12.611	88.867	7.350	4.756
4:4	4	4	0.298	29.5	74.3	11.820	2.029	30.600	4.756
6:6	6	6	1.214	61.2	65.6	7.442	27.300	65.600	4.756
1:1	1	1	0.362	43.7	77.6	7.583	43.700	75.400	4.697

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   10    11
chr  1.0  1.0  1.00 4.00  4.00  4.0 6.00  6.0  6.00 15.0 15.00
pos 43.7 72.4 88.87 2.03 29.87 74.3 7.35 27.3 60.65 19.1 35.55

Epistatic pairs by qtl, chr, pos:
  qtla qtlb chra chrb  posa  posb
1    9   10    6   15 60.65 19.10
2    6    9    4    6 74.30 60.65
3    6   11    4   15 74.30 35.55
4    2    5    1    4 72.40 29.87
5    2   10    1   15 72.40 19.10
6    3    7    1    6 88.87  7.35
7    4    5    4    4  2.03 29.87
8    8    9    6    6 27.30 60.65
9    1    2    1    1 43.70 72.40
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] 64

> 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@60.65 0.195 0.3650
2 Chr6@27.3            0.230 0.3240
3 Chr1@43.7:Chr1@72.4  0.211 0.3440
4 Chr4@2.03:Chr4@29.87 0.344 0.2260
5 Chr4@2.03            0.326 0.2370
6 Chr1@72.4:Chr15@19.1 0.327 0.2360
7 Chr1@72.4:Chr4@29.87 0.803 0.0625

> summary(cross.step$fit)

       df         SS        MS      LOD     %var Pvalue(Chi2) Pvalue(F)
Model  13  7569.678 582.28289 30.36511 42.84173            0         0
Error 236 10099.259  42.79347
Total 249 17668.936
```

Stepwise Reduction

	df	Type III SS	LOD	%var	F value	Pvalue(F)	
Chr1@43.7	1	280.841	1.489	1.589	6.563	0.011036	*
Chr1@72.4	1	440.048	2.315	2.491	10.283	0.001528	**
Chr1@88.87	2	369.779	1.952	2.093	4.321	0.014360	*
Chr4@29.87	1	2301.342	11.144	13.025	53.778	3.57e-12	***
Chr4@74.3	3	905.862	4.663	5.127	7.056	0.000146	***
Chr6@7.35	2	360.615	1.905	2.041	4.213	0.015923	*
Chr6@60.65	3	1886.117	9.295	10.675	14.692	8.37e-09	***
Chr15@19.1	2	1238.741	6.281	7.011	14.473	1.18e-06	***
Chr15@35.55	2	469.880	2.469	2.659	5.490	0.004672	**
Chr6@60.65:Chr15@19.1	1	1170.615	5.954	6.625	27.355	3.73e-07	***
Chr4@74.3:Chr6@60.65	1	356.905	1.885	2.020	8.340	0.004238	**
Chr4@74.3:Chr15@35.55	1	395.774	2.087	2.240	9.248	0.002623	**
Chr1@88.87:Chr6@7.35	1	348.260	1.840	1.971	8.138	0.004719	**

Reduced Genetic architecture

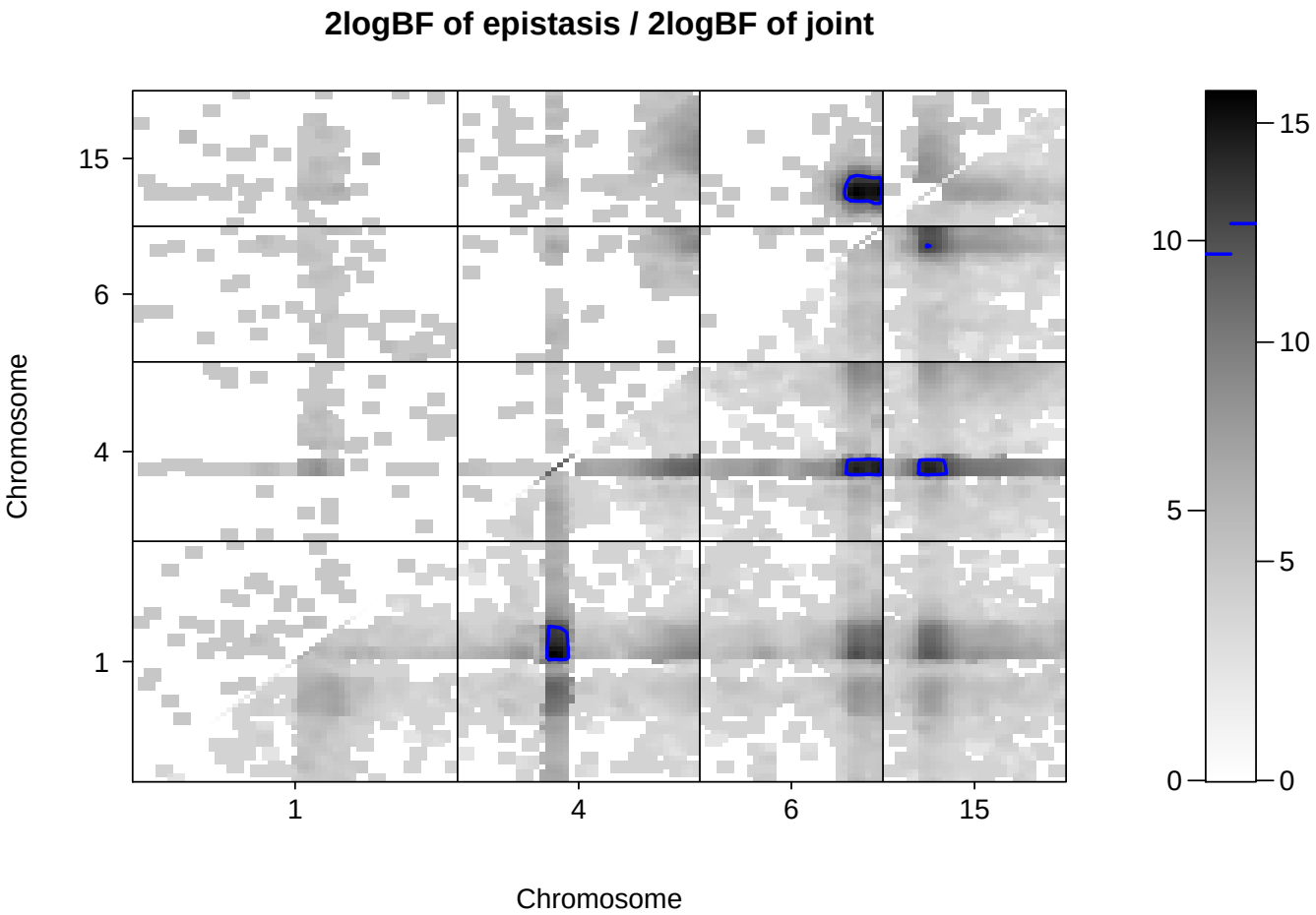
```
> cross.arch <- cross.step$arch
> cross.arch

main QTL loci:
       1    2     3     5    6    7     9   10    11
chr  1.0  1.0  1.00  4.00  4.0 6.00  6.00 15.0 15.00
pos 43.7 72.4 88.87 29.87 74.3 7.35 60.65 19.1 35.55

Epistatic pairs by qtl, chr, pos:
  q1 q2 chra chrb  posa  posb
1  9 10    6   15 60.65 19.10
2  6  9    4    6 74.30 60.65
3  6 11    4   15 74.30 35.55
4  3  7    1    6 88.87  7.35
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

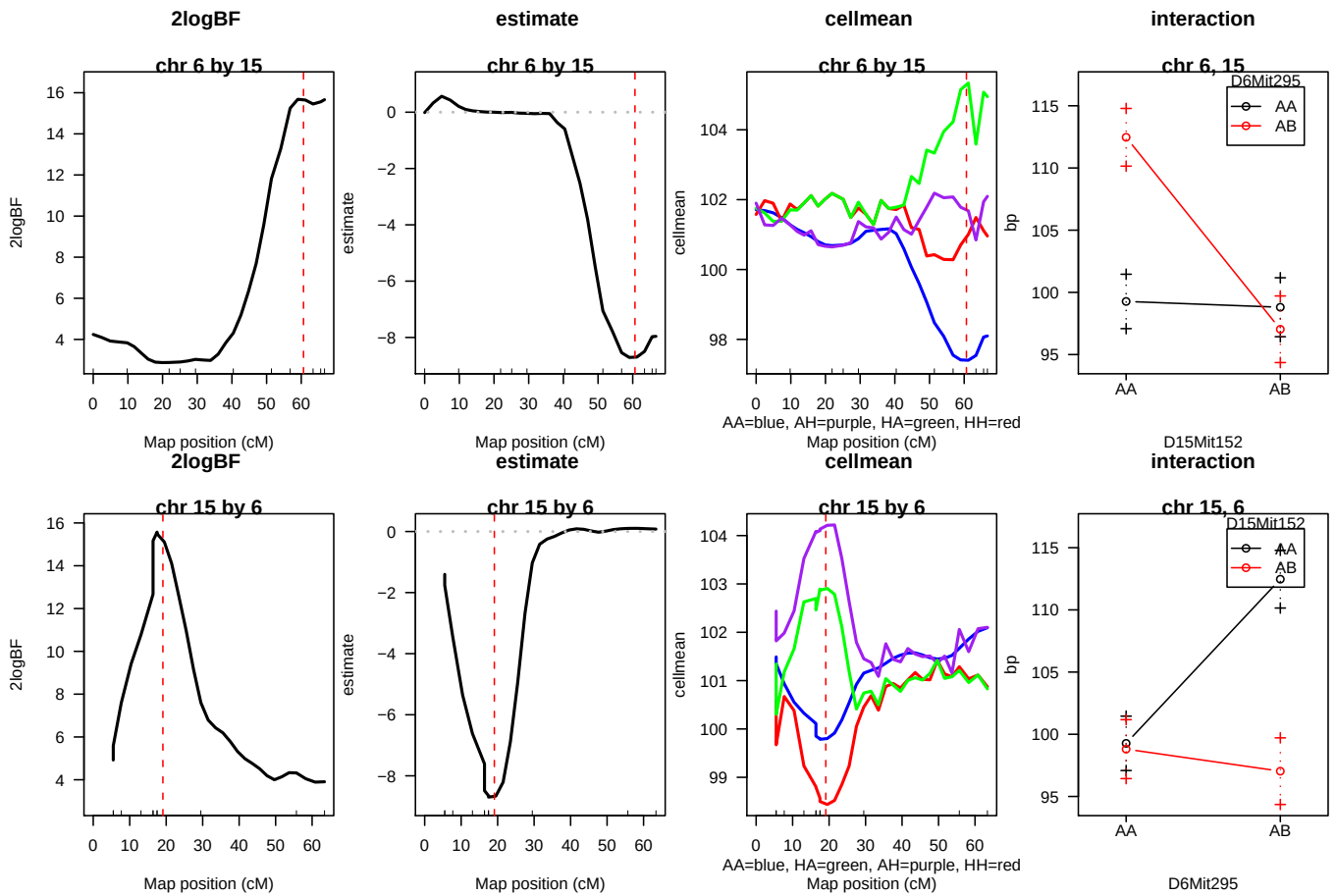


Slice Each Epistatic Pair

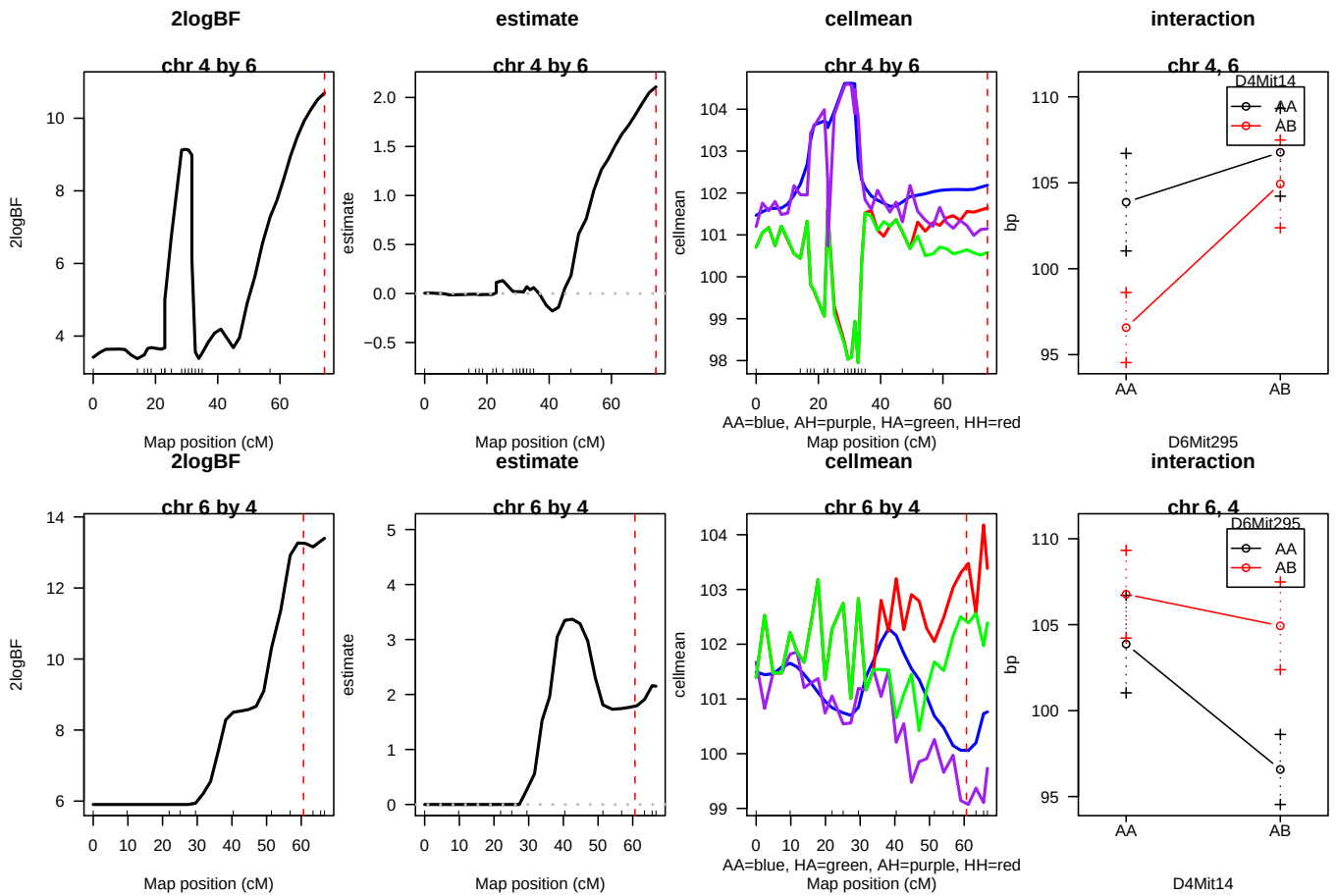
show detail plots for epistatic pairs (if any)

```
> 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))
+  }
+}
```

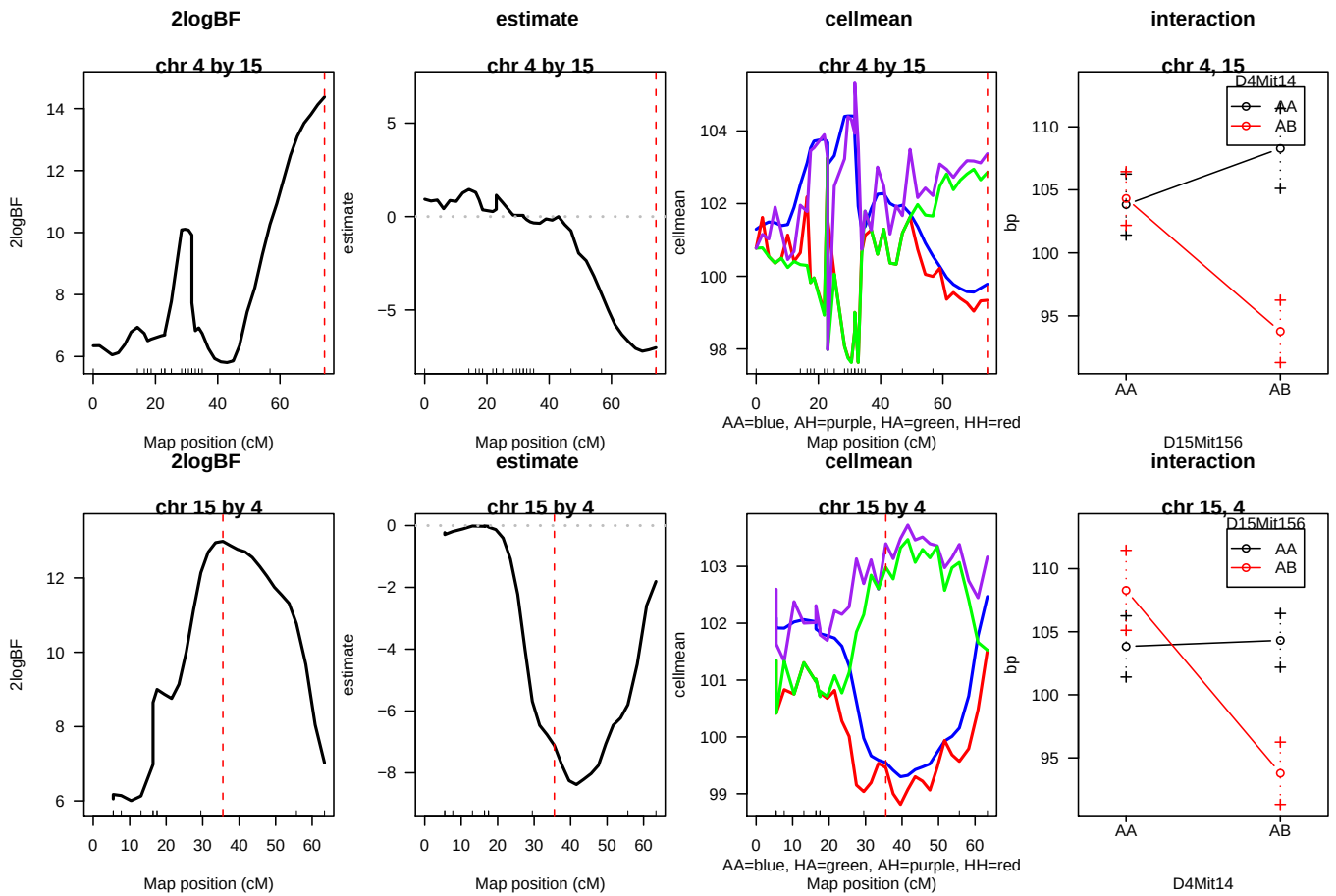
Epistatic Pair 6 and 15



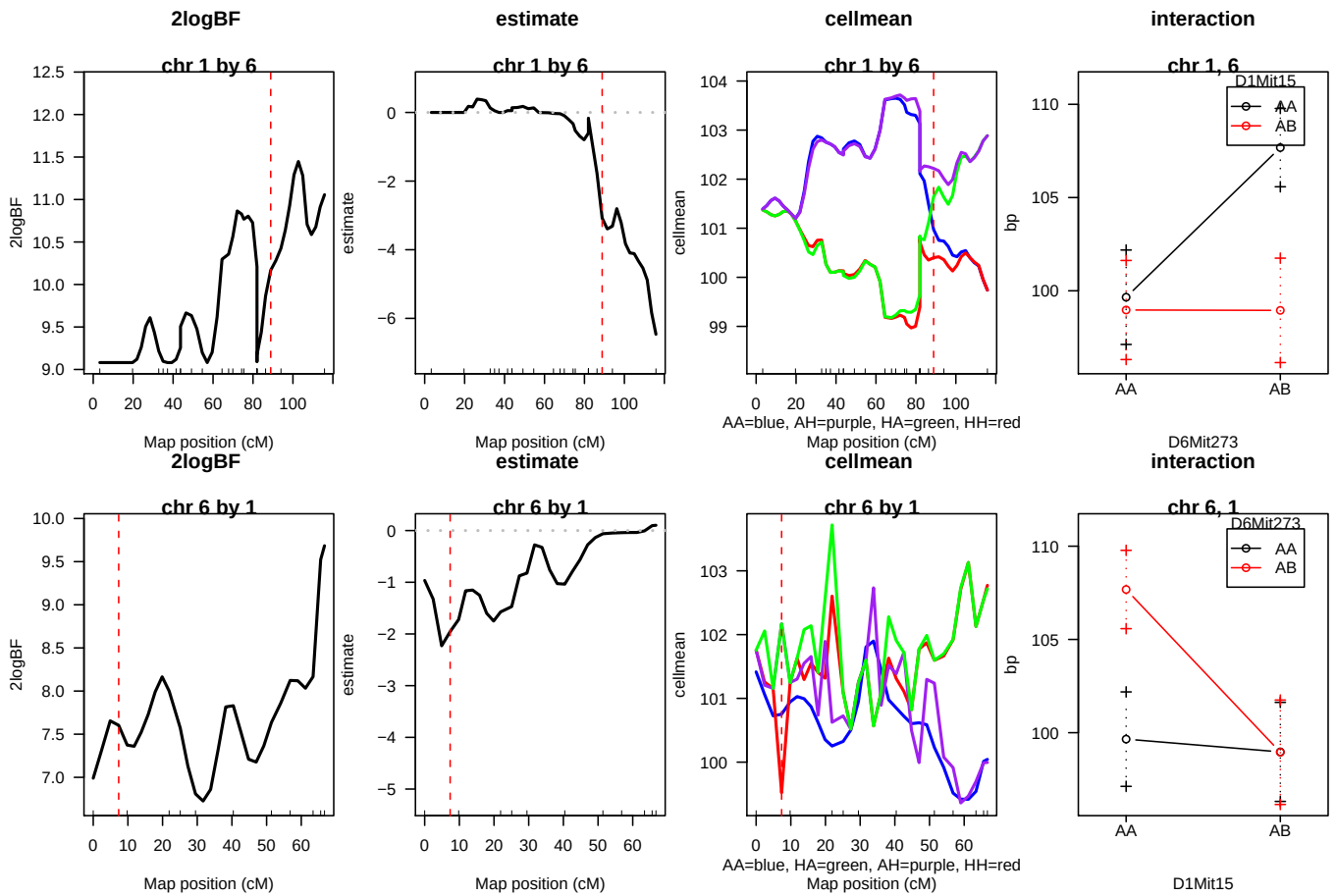
Epistatic Pair 4 and 6



Epistatic Pair 4 and 15



Epistatic Pair 1 and 6



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)
+ }
```