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 = 64,
+  scan.type = "2logBF", hpd.level = 0.5,
+  threshold = c(upper = 2),
+  SweaveFile = "/tmp/Rinst1076266882/qtlbim/doc/hyperslide.Rnw",
+  SweaveExtra = "/tmp/Rinst1076266882/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
```

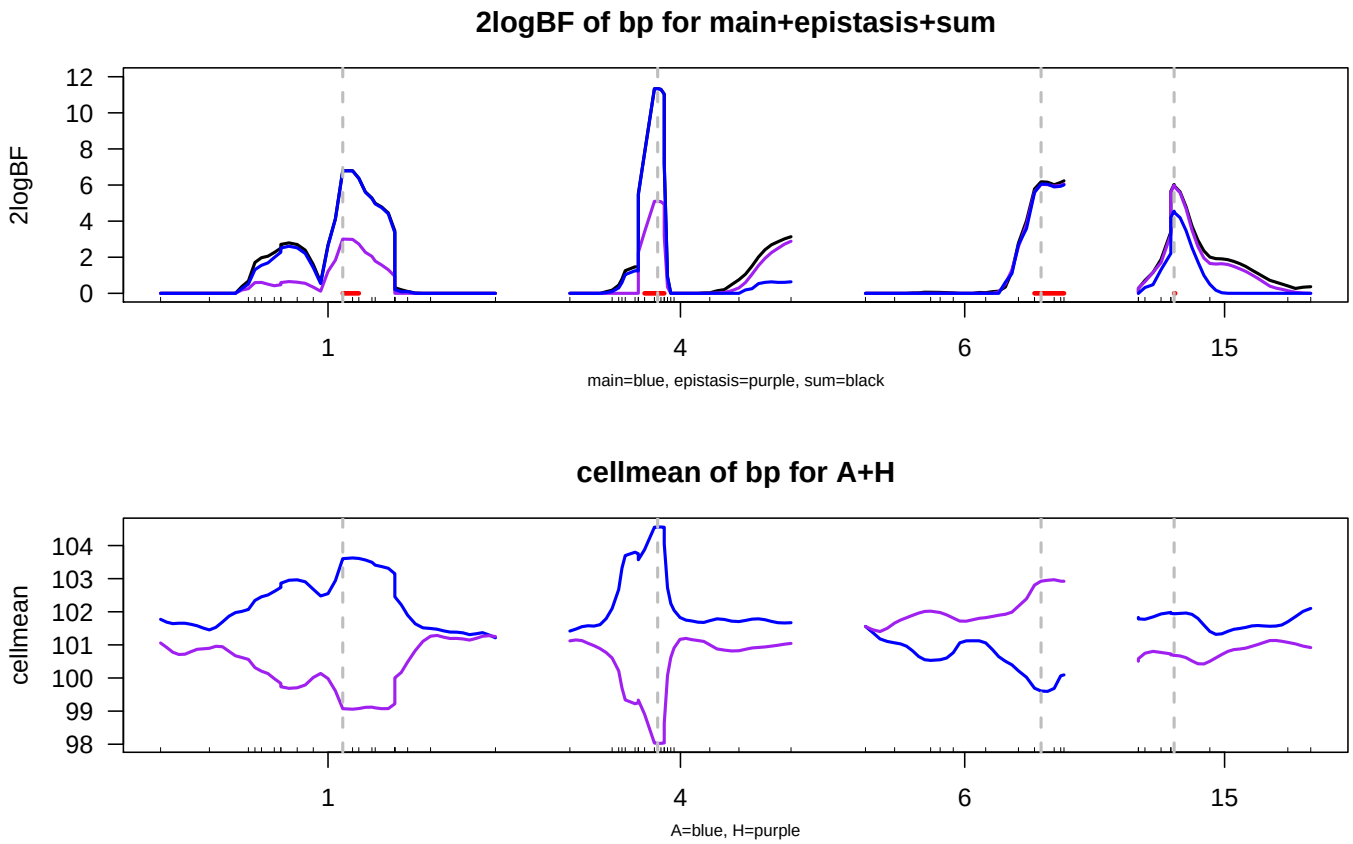
Create MCMC runs

```
> 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
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

     chr1 chr2 n.qtl l.pos1 l.pos2 lower u.pos1 u.pos2 upper
6.15    6   15  1.08     59   17.5 3.531     59   17.5 3.502
```

Initial Genetic Architecture

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

main QTL loci:
       1    2  3    4
chr  1.0  4.0  6 15.0
pos 64.5 29.5 59 17.5

Epistatic pairs by qtl, chr, pos:
  qtla qtlb chra chrb posa posb
1    3    4    6   15   59 17.5
Epistatic chromosomes by connected sets:
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)

> summary(cross.step$fit)

       df        SS         MS      LOD     %var Pvalue(Chi2) Pvalue(F)
Model   5  5483.571 1096.71428 20.17148 31.03510            0         0
Error 244 12185.365   49.94002
Total 249 17668.936
```

Stepwise Reduction

	df	Type III SS	LOD	%var	F value	Pvalue(F)	
Chr1@64.5	1	907.332	3.899	5.135	18.17	2.89e-05	***
Chr4@29.5	1	2795.609	11.213	15.822	55.98	1.32e-12	***
Chr6@59	2	1659.847	6.933	9.394	16.62	1.71e-07	***
Chr15@17.5	2	1478.142	6.215	8.366	14.80	8.58e-07	***
Chr6@59:Chr15@17.5	1	1192.735	5.069	6.750	23.88	1.86e-06	***

Reduced Genetic architecture

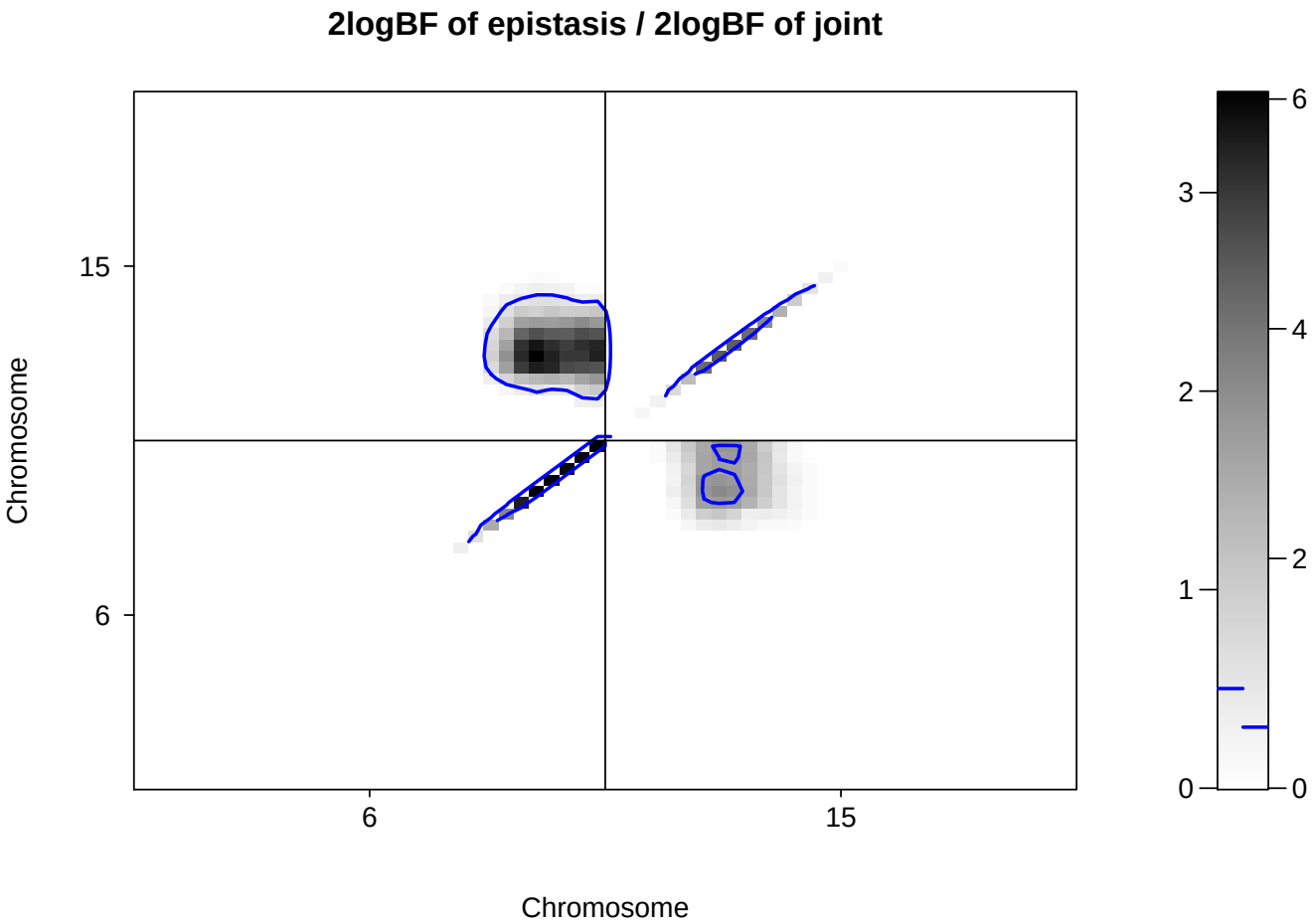
```
> cross.arch <- cross.step$arch
> cross.arch

main QTL loci:
       1    2  3    4
chr  1.0  4.0  6 15.0
pos 64.5 29.5 59 17.5

Epistatic pairs by qtl, chr, pos:
  q1 q2 chra chrb posa posb
1  3  4    6   15   59 17.5
Epistatic chromosomes by connected sets:
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

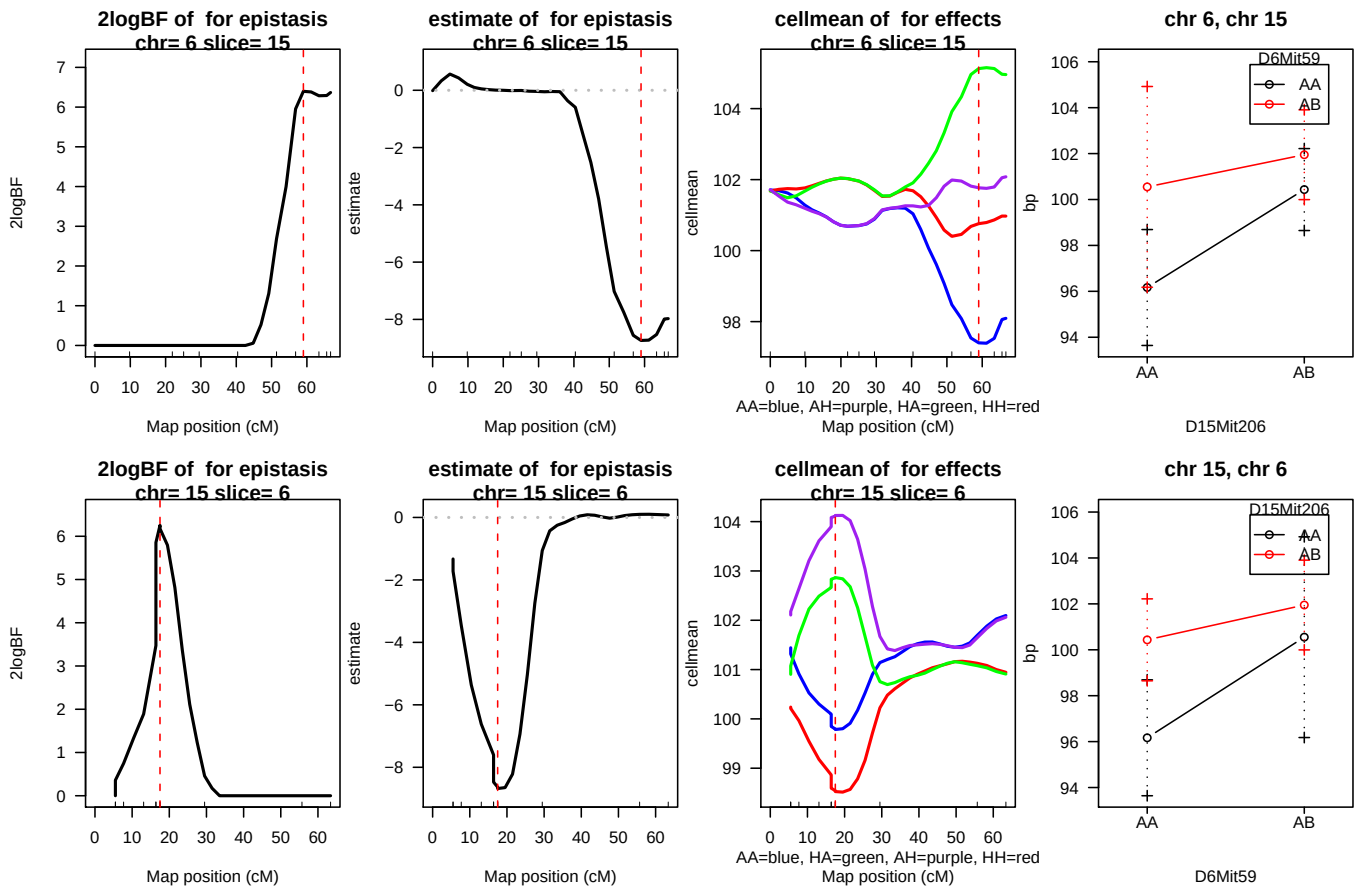


Slice Each Epistatic Pair

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



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)
+ }
```