

# Prototype QTL Strategy: Phenotype bp in Cross hyper

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## Overview

### Initialization

### 1-D & 2-D Scans

### Anova Fit

### User Customized Section

### Conclusion

# 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 = "",
+ SweaveExtra = "/tmp/RtmpcapCLa/Rinst16c77937e57/qtlbim/external/hyper.slide.extra.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 (%): BB:50.1 BA: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)
```

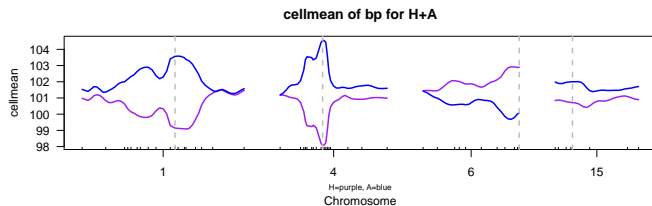
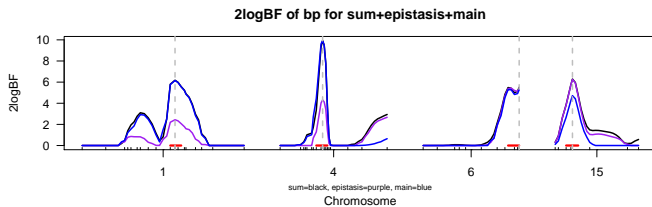
# 1-D 2logBF Scan

```
> hpd.level  
[1] 0.5  
  
> scan.type  
[1] "2logBF"  
  
> cross.hpd <- qb.hpdone(cross.qb, hpd.level, scan.type)  
> sum.one <- summary(cross.hpd)  
> sum.one  


|    | chr | n.qtl | pos  | lo.50. | hi.50. | 2logBF | A       | H       |
|----|-----|-------|------|--------|--------|--------|---------|---------|
| 1  | 1   | 0.695 | 67.8 | 64.5   | 72.1   | 6.181  | 103.568 | 99.143  |
| 4  | 4   | 2.834 | 29.5 | 25.1   | 32.8   | 9.924  | 104.550 | 98.078  |
| 6  | 6   | 0.743 | 66.7 | 59.0   | 66.7   | 5.488  | 99.710  | 102.866 |
| 15 | 15  | 0.909 | 17.5 | 13.1   | 21.5   | 6.291  | 101.999 | 100.710 |

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

# 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	1.004	66.7	17.5	11.44	66.7	17.5	11.43
c4 :c6	1.185	29.5	59.0	13.77	74.3	61.2	7.49
c4 :c15	1.452	29.5	17.5	13.28	74.3	47.6	6.84
c15:c15	0.261	21.5	23.5	7.12	17.5	31.5	6.21
c1 :c4	1.817	67.8	29.5	14.41	72.1	29.5	6.10
c1 :c6	1.103	67.8	59.0	11.37	67.8	59.0	5.21
c1 :c1	0.366	43.7	77.6	7.48	39.4	77.6	5.20
c1 :c15	1.255	67.8	17.5	10.87	75.4	23.5	4.76
c4 :c4	0.417	29.5	74.3	11.00	28.4	49.5	4.76
c6 :c6	0.111	61.2	65.6	7.52	40.4	56.8	3.94

# 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"	"1"	"15"	"15"	"4"	"4"	"4"	"6"	"6"
pos	"39.35"	"72.14"	"21.50"	"47.64"	"29.13"	"49.45"	"74.30"	"40.40"	"62.08"

Epistatic pairs by qtl, chr, pos:

	qtl	qtlb	chra	chrb	posa	posb
pair 1	3	9	15	6	21.50	62.08
pair 2	7	9	4	6	74.30	62.08
pair 3	4	7	15	4	47.64	74.30
pair 4	2	5	1	4	72.14	29.13
pair 5	2	9	1	6	72.14	62.08
pair 6	1	2	1	1	39.35	72.14
pair 7	2	3	1	15	72.14	21.50
pair 8	5	6	4	4	29.13	49.45
pair 9	8	9	6	6	40.40	62.08

Epistatic chromosomes by connected sets:

1,15,4,6

## Construct QTL Object

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

```
> cross.sub <- subset(cross, chr = unique(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, as.character(cross.arch$qtl$chr), cross.arch$qtl$pos)
```

# Stepwise Reduction

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

	drop	LOD	p
1	1039.3:1071.3	-0.0450	1.0000
2	1039.3:1071.3	0.1450	0.4310
3	1039.3:1071.3	0.1990	0.3550
4	4029.5:4050.0	0.0862	0.5420
5	4050.0	0.0623	0.6040
6	1071.3:15021.5	0.1380	0.4390
7	1071.3:15021.5	0.1400	0.4350
8	1071.3:15021.5	0.1310	0.4490
9	1071.3:15021.5	0.1650	0.3940
10	15047.5	0.2770	0.2690
11	6040.4:6062.0	0.4140	0.1760
12	6040.4	0.1310	0.4460
13	4074.3	0.8090	0.0573

```
> summary(cross.step$fit)
```

	df	SS	MS	LOD	%var	Pvalue(Chi2)	Pvalue(F)
Model	5	4853.771	970.75417	17.43577	27.47065	7.771561e-16	1.44329e-15
Error	244	12815.166	52.52117				
Total	249	17668.936					

# Stepwise Reduction

	df	Type	III SS	LOD	%var	F value	Pvalue(F)	
1@39.3	1		303.8	1.272	1.719	5.784	0.01692	*
1@71.3	1		565.2	2.343	3.199	10.762	0.00119	**
15@21.5	1		314.9	1.318	1.782	5.995	0.01505	*
4@29.5	1		2752.1	10.561	15.576	52.401	5.87e-12	***
6@62.0	1		427.8	1.783	2.421	8.145	0.00469	**

## Reduced Genetic architecture

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

main QTL loci:
   1      2      3      5      9
chr "1"   "1"   "15"  "4"   "6"
pos "39.35" "72.14" "21.50" "29.13" "62.08"

epistatic pairs: none
```

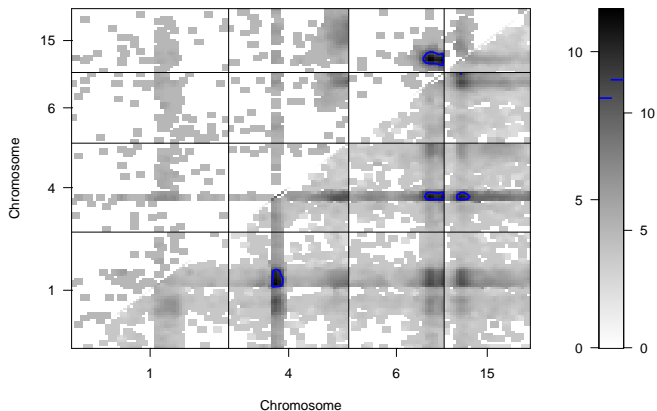
## 2-D Plots

### 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

2logBF of epistasis / 2logBF of full



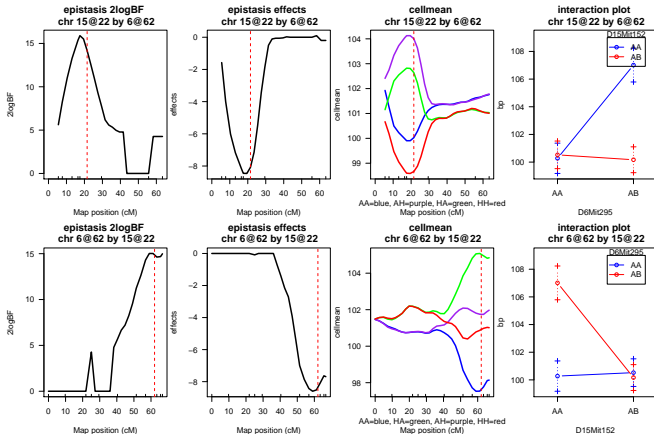


## Slice Each Epistatic Pair

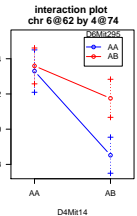
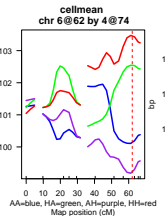
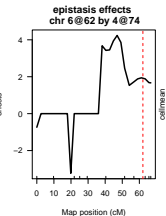
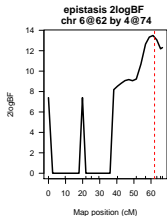
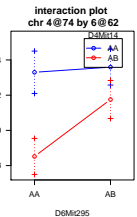
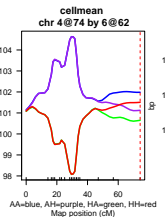
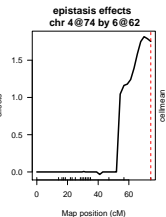
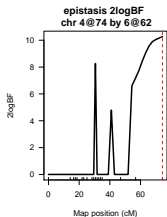
show detail plots for epistatic pairs (if any)

```
> 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,]  
+     if(chri[1] != chri[2])  
+       plot(qb.slicetwo(cross.qb, chri, posi, scan.type))  
+   }  
+}
```

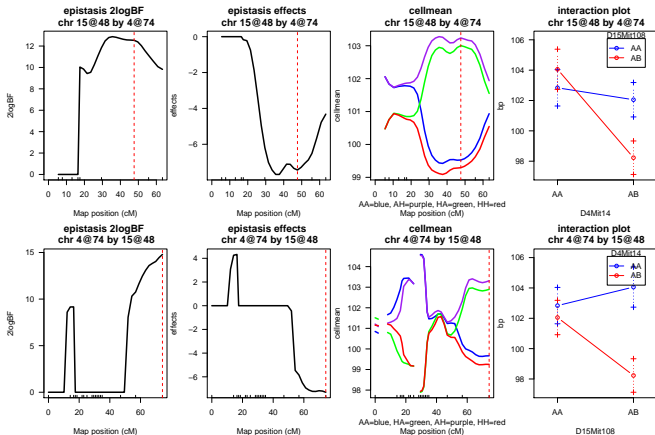
# Epistatic Pair 15 and 6



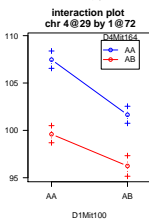
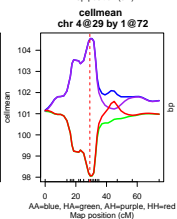
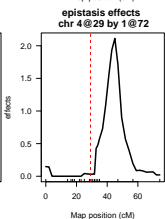
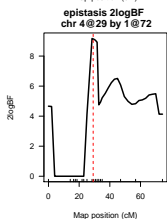
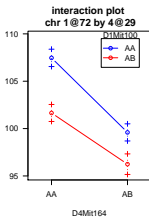
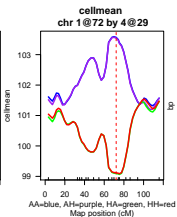
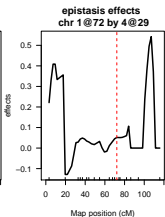
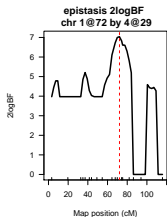
# Epistatic Pair 4 and 6



# Epistatic Pair 15 and 4

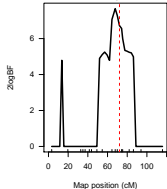


# Epistatic Pair 1 and 4

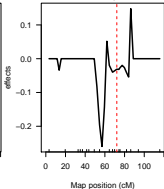


# Epistatic Pair 1 and 6

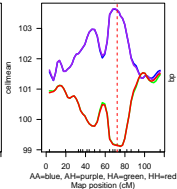
**epistasis 2logBF**  
chr 1@72 by 6@62



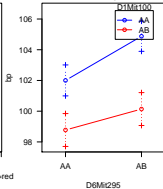
**epistasis effects**  
chr 1@72 by 6@62



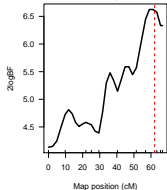
**cellmean**  
chr 1@72 by 6@62



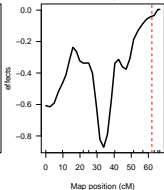
**interaction plot**  
chr 1@72 by 6@62



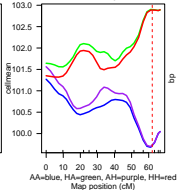
**epistasis 2logBF**  
chr 6@62 by 1@72



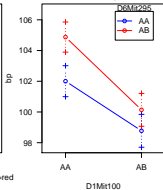
**epistasis effects**  
chr 6@62 by 1@72



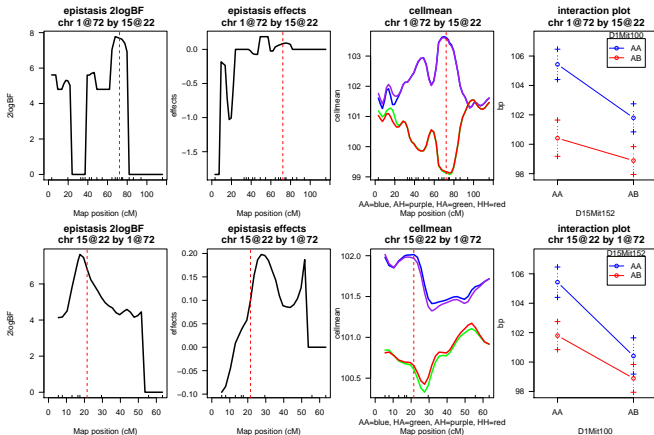
**cellmean**  
chr 6@62 by 1@72



**interaction plot**  
chr 6@62 by 1@72



# Epistatic Pair 1 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 .tex to bp.tex

and run pdflatex twice on it

remove objects created by R/qt1bim if desired

```
> file.rename(".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)
+ }
```