Prototype QTL Strategy: Phenotype bp in Cross hyper

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Overview
1-D & 2-D Scans
Anova Fit
User Customized Section
Conclusion

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Initialization

Automated Strategy

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

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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/Rinst3044321515/qtlbim/external/hyper.slide.extra.Rnw",
+  PDFDir = "bpPDF",
+  remove.qb = TRUE)
```

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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
```

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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 0.826 67.8   64.5   74.3  6.181 103.568  99.143
4     4 3.035 29.5   23.0   31.7  9.970 104.552  98.073
6     6 0.873 66.7   56.8   66.7  5.488  99.710 102.866
15   15 0.395 17.5   17.5   19.5  5.448 101.993 100.703

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

> plot(cross.hpd)
```
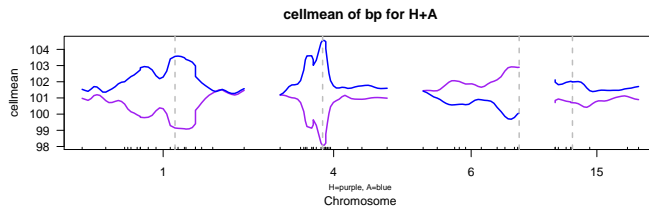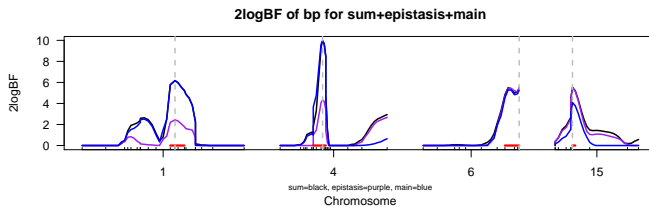
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1-D Scan: 2logBF Profile

2logBF of bp for sum+epistasis+main

cellmean of bp for H+A

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   59.0   17.5 11.89   59.0   17.5 11.90
c4 :c6  1.185   29.5   59.0 13.77   74.3   61.2  7.49
c4 :c15 1.452   29.5   17.5 13.61   74.3   47.6  6.84
c15:c15 0.261   17.5   33.5  7.54   17.5   31.5  6.52
c1 :c4  1.817   67.8   29.5 14.41   72.1   29.5  6.10
c1 :c15 1.255   67.8   17.5 11.20   72.1   17.5  5.23
c1 :c6  1.103   67.8   59.0 11.37   67.8   59.0  5.21
c1 :c1  0.366   43.7   77.6  7.46   39.4   77.6  5.20
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"     "15"     "4"      "4"      "4"      "6"
pos "39.35" "71.48"  "17.50"  "31.52"  "47.64"  "29.13"  "49.45"  "74.30"  "40.40"
    [,10]
chr "6"
pos "60.54"

Epistatic pairs by qtl, chr, pos:
        qtla qtlb chra chrb  posa  posb
pair 1     3   10   15     6 17.50 60.54
pair 2     8   10   15     4 74.30 60.54
pair 3     5    8   15     4 47.64 74.30
pair 4     3    4   15    15 17.50 31.52
pair 5     2    6    1     4 71.48 29.13
pair 6     2    3    1    15 71.48 17.50
pair 7     2   10    1     6 71.48 60.54
pair 8     1    2    1     1 39.35 71.48
pair 9     6    7    4     4 29.13 49.45
pair 10    9   10    6     6 40.40 60.54
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)
> cross.sub <- clean(cross.sub)
```

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Stepwise Reduction

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

    drop                   LOD      p
1   Chr6@40.4:Chr6@60     -0.84700 1.0000
2   Chr1@71.3:Chr15@17.5   0.02990 0.7220
3   Chr1@71.3:Chr15@17.5   0.00441 0.8910
4   Chr4@29.5:Chr4@50      0.00830 0.8510
5   Chr4@50               -0.14200 1.0000
6   Chr15@47.5             0.16500 0.4000
7   Chr6@40.4              0.18700 0.3690
8   Chr1@71.3:Chr4@29.5    0.46600 0.1550
9   Chr1@71.3:Chr15@17.5   0.62900 0.0978
10  Chr15@31.5             0.03770 0.6850
11  Chr1@71.3:Chr6@60      0.23700 0.3070
12  Chr1@71.3:Chr15@17.5   0.29000 0.2580
13  Chr4@74.3              0.62000 0.0974
14  Chr1@39.3:Chr1@71.3    0.81900 0.0563
15  Chr1@39.3:Chr1@71.3    0.51200 0.1300

> summary(cross.step$fit)

        df       SS        MS       LOD    %var Pvalue(Chi2)    Pvalue(F)
Model    5  4844.618 968.92358 17.39701 27.41884 7.771561e-16 1.554312e-15
Error  244 12824.318  52.55868
Total  249 17668.936
```

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```
            df Type III SS      LOD    %var F value Pvalue(F)
Chr1@39.3    1     282.101    1.181   1.597   5.367 0.021346 *
Chr1@71.3    1     587.964    2.434   3.328  11.187 0.000954 ***
Chr15@17.5   1     310.687    1.299   1.758   5.911 0.015766 *
Chr4@29.5    1    2754.251   10.562  15.588  52.403 5.86e-12 ***
Chr6@60      1     463.118    1.926   2.621   8.811 0.003291 **
```

Reduced Genetic architecture

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

main QTL loci:
    1       2       3       6       10
chr "1"     "1"     "15"    "4"     "6"
pos "39.35" "71.48" "17.50" "29.13" "60.54"

epistatic pairs: none
```
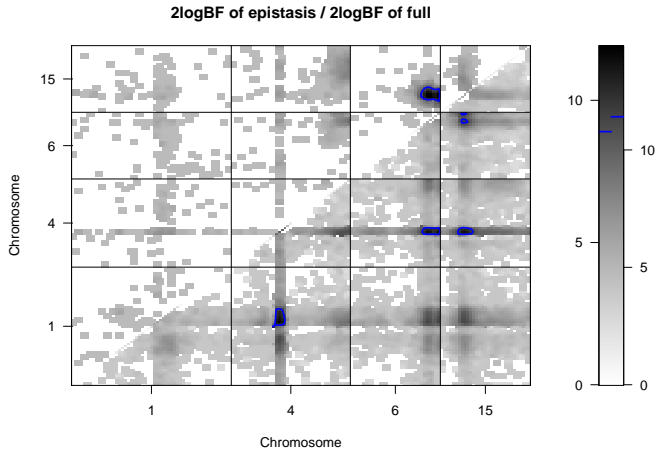
2-D Plots

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)
```
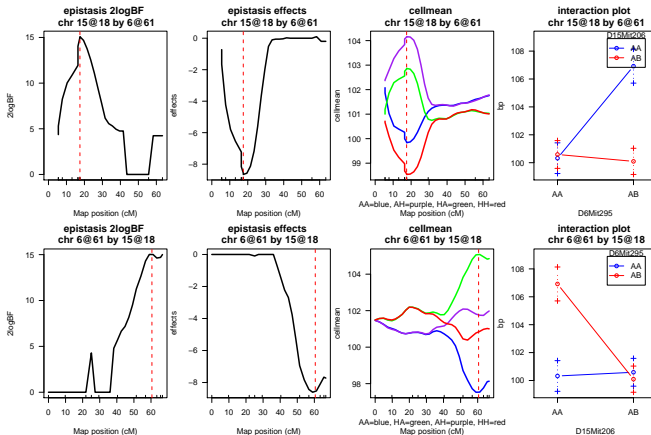
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2-D Plots: clique 1

2logBF of epistasis / 2logBF of full

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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))
+ }
+}
```
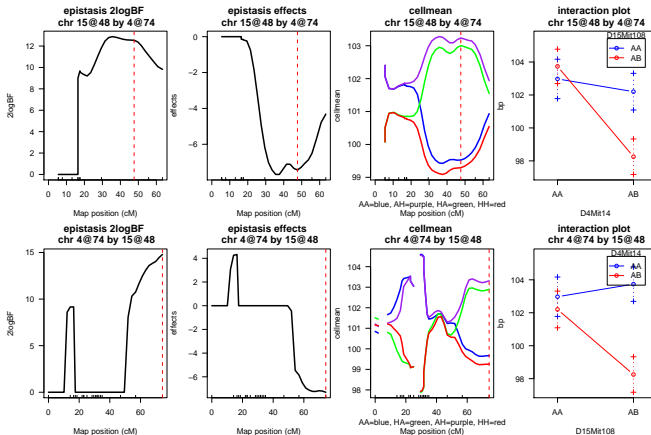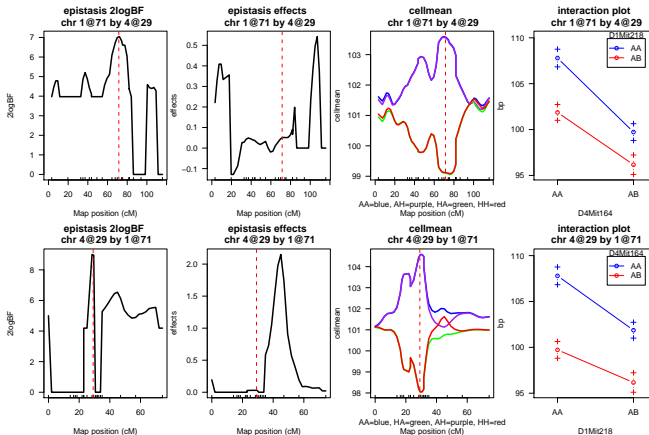
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Epistatic Pair 15 and 6

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Epistatic Pair 4 and 6

Epistatic Pair 15 and 4

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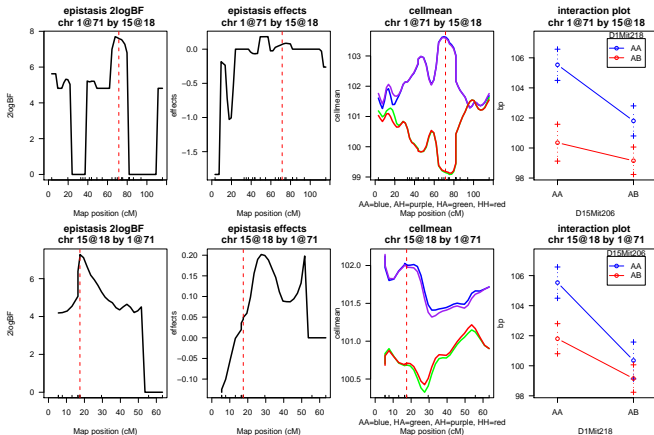Overview
1-D & 2-D Scans
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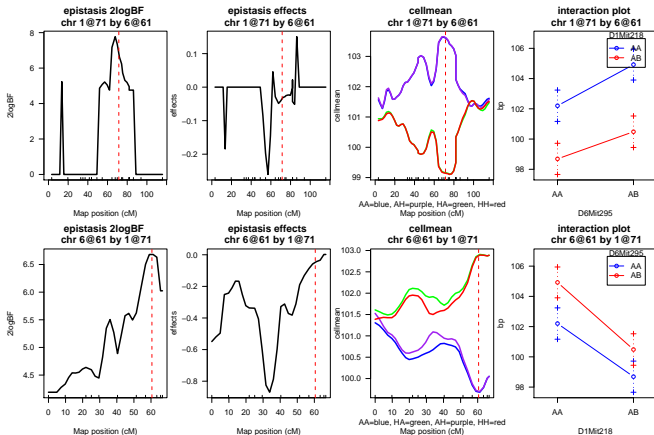User Customized Section
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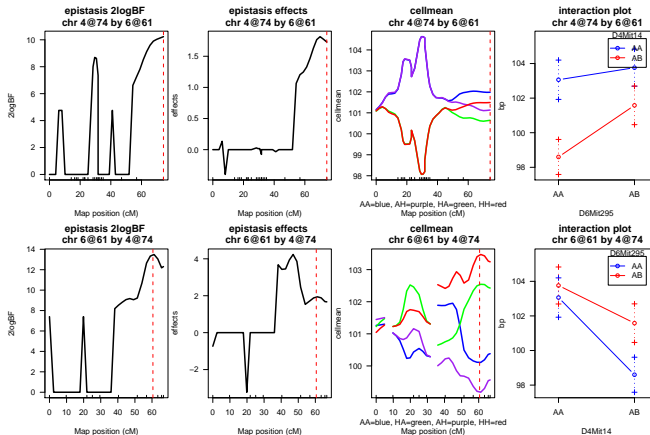
Epistatic Pair 1 and 4

Epistatic Pair 1 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
```

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Sugiyama Model

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

> summary(cross.step2$fit)
```

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Sugiyama vs. Automata

formal comparison with automated model

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

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final tasks:

externally rename file .tex to bp.tex

and run pdflatex twice on it

remove objects created by R/qtlbim 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)
+ }
```