

Prototype QTL Strategy: Phenotype bp in Cross hyper

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

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Overview

Initialization

1-D & 2-D Scans

Anova Fit

Epistasis Plots

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(bmqtl)

> bmq.sweave(hyper, pheno.col = 1,
+ n.iter = 3000, n.draws = 64,
+ threshold = c(main = 3, epistasis = 3, upper = 2),
+ maxpairs = c(20, 5),
+ SweaveFile = /u/y/a/yandell/public/statgen/R/bmqtl/doc/hyperslide.Rnw,
+ SweaveExtra = ,
+ PDFDir = bpPDF,
+ remove.bmq = FALSE)
```

Cross Object

```
> summary(cross)
```

```
Backcross
```

```
No. individuals: 250
```

```
No. phenotypes: 1
```

```
Percent phenotyped: 100
```

```
No. chromosomes: 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 <- bmq.genoprob(cross, step = 2)
> cross.bmq <- bmq.mcmc(cross, genoupdate=TRUE, n.iter = 3000)
```

Bayesian MCMC run in progress. The current saved iterations:

200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
2600
2800
3000

MCMC sample has been saved to: ./bp_May-24-114447.

Bayesian MCMC took 10.37 minutes.

1-D LOD Scan

```
> one <- bscanone(cross.bmq, type = "LOD")  
> sum.one <- summary(one, threshold = threshold, sort = "sum")  
> sum.one
```

	chr	pos	main	epistasis	sum	niter
4	4	29.500	10.983	4.744	11.099	4149
6	6	61.200	3.851	4.637	7.579	1612
1	1	67.800	6.315	2.109	6.462	4054
15	15	27.500	1.754	5.786	6.361	1957
11	11	43.700	0.856	4.837	5.166	519
18	18	12.200	1.001	4.001	4.047	208
3	3	26.256	1.348	3.380	3.785	513
7	7	41.300	0.693	3.446	3.480	583
12	12	25.175	1.357	3.409	3.443	337
13	13	59.000	0.583	3.326	3.366	290
2	2	42.633	3.098	2.584	3.271	1563

1-D Scan: Positions of Main QTL

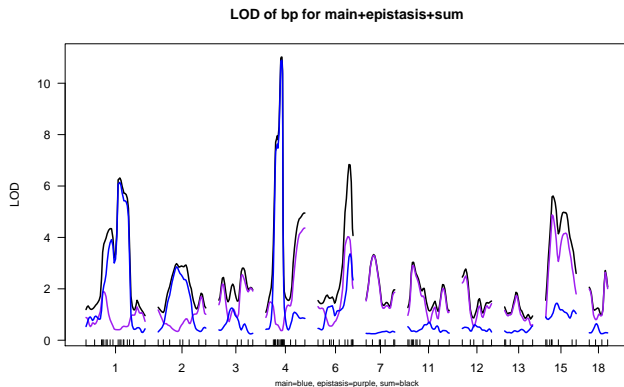
```
> chrs <- sort(as.vector(sum.one[, "chr"]))  
> pos <- sum.one[as.character(chrs), "pos"]  
> pos
```

```
      1      2      3      4      6      7      11      12      13      15      18  
67.800 42.633 26.256 29.500 61.200 41.300 43.700 25.175 59.000 27.500 12.200
```

plot key chromosomes on next slide

```
> plot(one, chr = chrs, smooth = 3)
```


1-D Scan: LOD Profile



1-D Scan: Cell Mean Profile

```
> tmp <- sum.one[as.character(chrs), "main"] >= threshold["main"]  
> chr1 <- chrs[tmp]  
> one <- bscanone(cross.bmq, chr = chr1, type = "cellmean")  
> summary(one)
```

	chr	pos	A	H	niter
1	1	66.062	103.076	99.371	4054
2	2	50.705	102.264	100.120	1563
4	4	35.683	103.681	98.805	4149
6	6	49.945	100.241	102.266	1612

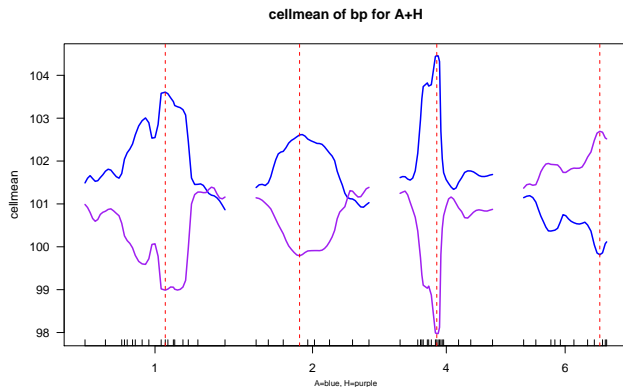
technical device to add vertical line at max LOD:

```
> pos1 <- pos[tmp]  
> pos.plot <- map.pos(cross, chr1, pos1)  
> pos.plot
```

	1	2	4	6
	64.500	172.433	282.700	413.700

```
> plot(one, smooth = 3)  
> abline(v = pos.plot, lty = 2, col = "red")
```

1-D Scan: Cell Mean Profile



2-D: find epistatic pairs

```
> two <- bscantwo(cross.bmq, chr = chrs, type = "LOD")
> maxpairs
[1] 20 5
> sum.two <- summary(two, sort = "upper", threshold = threshold,
+   maxpairs = maxpairs[1])
> sum.two
```

	chr1	chr2	pos1	pos2	lower	upper	niter
3.15	3	15	10.943	63.400	17.063	7.057	366
11.11	11	11	33.367	64.260	15.193	5.577	814
4.15	4	15	74.300	41.592	14.451	5.544	178
6.11	6	11	66.700	66.340	10.675	5.306	125
1.7	1	7	35.000	17.467	16.167	5.228	420
2.3	2	3	60.650	60.100	12.361	3.759	279
11.12	11	12	29.233	48.600	11.792	3.678	536
4.6	4	6	67.737	42.600	12.526	3.414	348
1.6	1	6	104.900	2.450	13.979	3.250	2115
6.15	6	15	51.400	23.500	13.261	3.246	380
3.13	3	13	30.633	27.309	12.731	3.052	298
3.11	3	11	13.129	70.500	12.729	2.764	4
4.18	4	18	14.200	2.200	10.742	2.732	159
7.11	7	11	37.200	19.700	11.551	2.660	421
1.1	1	1	30.617	30.617	12.829	2.618	1182
2.13	2	13	42.633	22.945	15.052	2.415	555
3.7	3	7	46.983	53.600	10.792	2.319	324
12.13	12	13	18.600	50.733	9.382	2.276	343

Initial Genetic Architecture

```
> arch <- bmq.mergeqtl(chrs, pos, sum.two)
> t(arch$qtl)

      1    2    3    4    5    6    7    8    9   10   11   12   13
chr  1.00  1.0  1.0  2.00  2.00  3.00  3.00  3.00  3.0  4.0  4.0  4.00  6.00
pos 32.08 67.8 104.9 42.63 60.65 12.04 28.44 46.98 60.1 14.2 29.5 71.02 2.45
      14   15   16   17   18   19   20   21   22   23   24   25   26
chr  6.00  7.00  7.00  7.0 11.00 11.0 11.00 12.00 12.0 13.00 13.00 15.0 15.00
pos 55.47 17.47 39.25 53.6 27.43 43.7 67.03 21.89 48.6 25.13 54.87 25.5 41.59
      27   28
chr 15.0 18.0
pos 63.4  7.2

> if (!is.null(arch$pairs)) t(arch$pairs)

      1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17
q1  6 18 12 14  1 5 18 12  3 14  7  6 10 16  4  8 21
q2 27 20 26 20 15 9 22 14 13 25 23 20 28 18 23 17 24

pairs (if any) index the qtl list
archpairs shows chromosome pairs

> archpairs <- bmq.archpairs(arch)
> if (!is.null(archpairs)) t(archpairs$chr)

      1  2  3  4 5 6  7 8 9 10 11 12 13 14 15 16 17
q1  3 11  4  6 1 2 11 4 1  6  3  3  4  7  2  3 12
q2 15 11 15 11 7 3 12 6 6 15 13 11 18 11 13  7 13
```

Construct QTL Object

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

```
> cross <- calc.genoprob(clean(cross), step = 2, error = 0.01)  
> n.draws
```

```
[1] 64
```

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

Stepwise Reduction

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

	drop	LOD	p
1	Chr4@14.2:Chr18@7.2	0.0486	0.6690
2	Chr3@46.98:Chr7@53.6	0.1340	0.4780
3	Chr12@21.89:Chr13@54.87	0.1940	0.3910
4	Chr12@21.89	0.1550	0.4420
5	Chr18@7.2	0.1850	0.4010
6	Chr6@55.47:Chr11@67.03	0.1710	0.4180
7	Chr3@12.04:Chr11@67.03	0.2590	0.3170
8	Chr7@53.6	0.3630	0.2350
9	Chr4@14.2	0.3540	0.2400
10	Chr3@46.98	0.4040	0.2090
11	Chr2@42.63:Chr13@25.13	0.3870	0.2170
12	Chr2@42.63	0.2370	0.3330
13	Chr1@104.9:Chr6@2.45	0.6960	0.0964
14	Chr6@2.45	0.2580	0.3110
15	Chr1@104.9	0.3250	0.2540
16	Chr13@54.87	0.7330	0.0859
17	Chr7@39.25:Chr11@27.43	0.6860	0.0959
18	Chr7@39.25	0.4700	0.1670
19	Chr11@27.43:Chr12@48.6	0.6970	0.0917
20	Chr12@48.6	0.2890	0.2770
21	Chr11@43.7	0.6830	0.0937
22	Chr3@28.44:Chr13@25.13	1.3700	0.0172
23	Chr13@25.13	0.1280	0.4650
24	Chr3@28.44	0.6430	0.1010

Stepwise Reduction

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

	df	SS	MS	LOD	%var	Pvalue(Chi2)	Pvalue(F)
Model	15	7486.293	499.08617	29.91873	42.3698	0	0
Error	234	10182.644	43.51557				
Total	249	17668.936					

Stepwise Reduction

	df	Type III SS	LOD	%var	F value	Pvalue(Chi2)
Chr1@32.08	2	492.474	2.564	2.787	5.659	0.003
Chr1@67.8	1	881.071	4.505	4.987	20.247	5.24e-06
Chr3@12.04	2	648.405	3.351	3.670	7.450	4.45e-04
Chr4@29.5	1	2532.407	12.057	14.333	58.195	9.23e-14
Chr4@71.02	3	1012.395	5.146	5.730	7.755	2.89e-05
Chr6@55.47	3	1520.195	7.554	8.604	11.645	1.35e-07
Chr7@17.47	2	401.057	2.097	2.270	4.608	0.008
Chr15@25.5	2	818.464	4.197	4.632	9.404	6.35e-05
Chr15@41.59	2	531.613	2.763	3.009	6.108	0.002
Chr15@63.4	2	625.334	3.235	3.539	7.185	0.001
Chr3@12.04:Chr15@63.4	1	536.253	2.786	3.035	12.323	3.41e-04
Chr4@71.02:Chr15@41.59	1	473.191	2.466	2.678	10.874	0.001
Chr1@32.08:Chr7@17.47	1	390.505	2.043	2.210	8.974	0.002
Chr4@71.02:Chr6@55.47	1	438.419	2.288	2.481	10.075	0.001
Chr6@55.47:Chr15@25.5	1	714.923	3.684	4.046	16.429	3.81e-05

Pvalue(F)

Chr1@32.08	0.003982 **
Chr1@67.8	1.07e-05 ***
Chr3@12.04	0.000730 ***
Chr4@29.5	5.95e-13 ***
Chr4@71.02	5.85e-05 ***
Chr6@55.47	3.86e-07 ***
Chr7@17.47	0.010892 *
Chr15@25.5	0.000118 ***
Chr15@41.59	0.002595 **

Reduced Genetic architecture

```
> arch2 <- cross.step$arch
> t(arch2$qt1)

      1   2   6  11  12  14  15  25  26  27
chr  1.00 1.0 3.00 4.0 4.00 6.00 7.00 15.0 15.00 15.0
pos  32.08 67.8 12.04 29.5 71.02 55.47 17.47 25.5 41.59 63.4

> if (!is.null(arch2$pairs)) t(arch2$pairs)

      1  2  3  4  5
q1  6 12  1 12 14
q2  27 26 15 14 25

above pairs index the qtl list
pairs below show chromosome pairs

> archpairs <- bmq.archpairs(arch2)
> if (!is.null(archpairs)) t(archpairs$chr)

      1  2  3  4  5
q1  3  4  1  4  6
q2 15 15  7  6 15
```

2-D Pairs

now find the chromosomes involved in pairs
group chromosomes by connection clique

```
> chr2 <- bmq.pairgroup(arch2)  
> chr2
```

```
[[1]]  
[1] 3 4 6 15
```

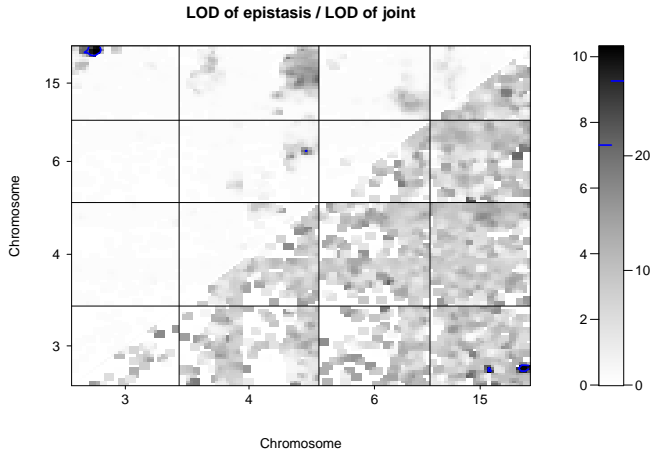
```
[[2]]  
[1] 1 7
```

2-D Plots

2-D plots by cliques (if any epistasis)

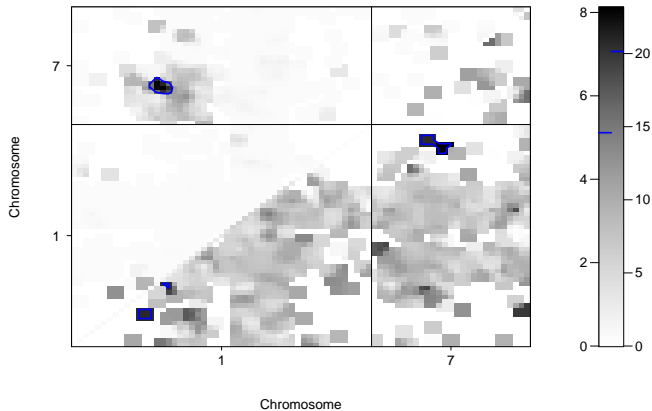
```
> cross <- bmq.genoprob(cross, step = 2)
> if(length(chr2)) {
+   for(i in seq(length(chr2)))
+     plot(two, chr = chr2[[i]], smooth = 3,
+         col = "gray", contour = 3)
+ }
```

2-D Plots: clique 1



2-D Plots: clique 2

LOD of epistasis / LOD of joint

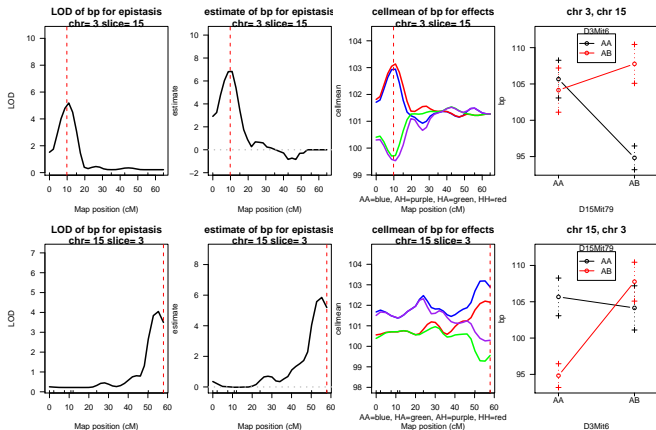


Slice Each Epistatic Pair

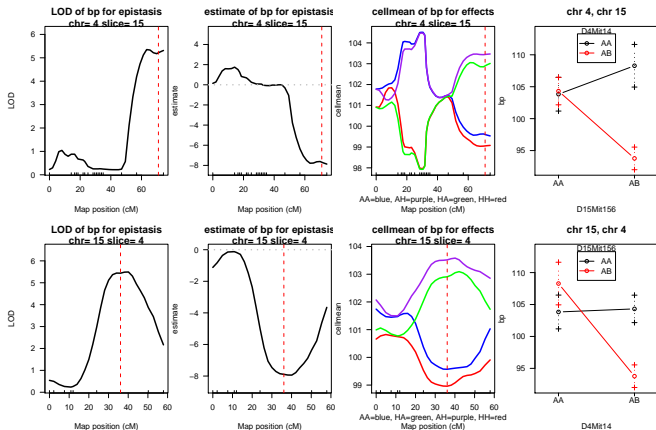
show detail plots for epistatic pairs (if any)

```
> if(length(chr2)) {  
+   for(i in seq(nrow(archpairs$chr))) {  
+     chri <- archpairs$chr[i,]  
+     posi <- archpairs$pos[i,]  
+     bmq.showtwo(cross.bmq, chri, posi)  
+   }  
+}
```

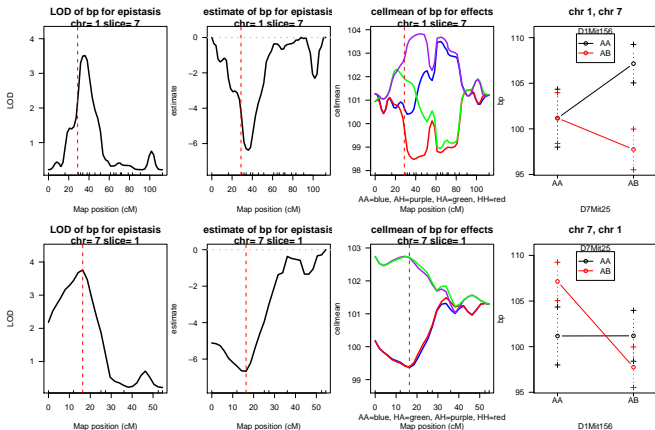
Epistatic Pair 3 and 15



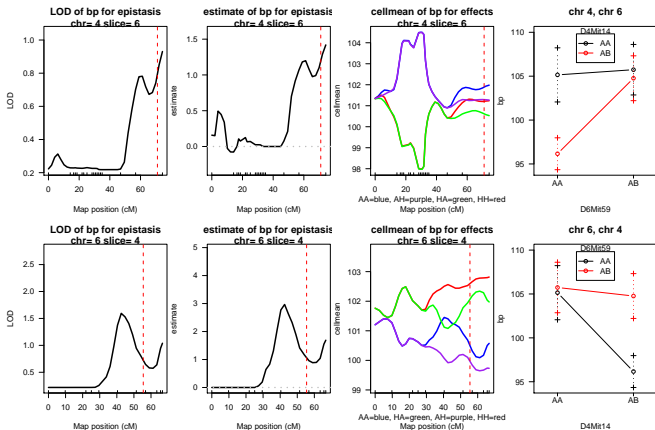
Epistatic Pair 4 and 15



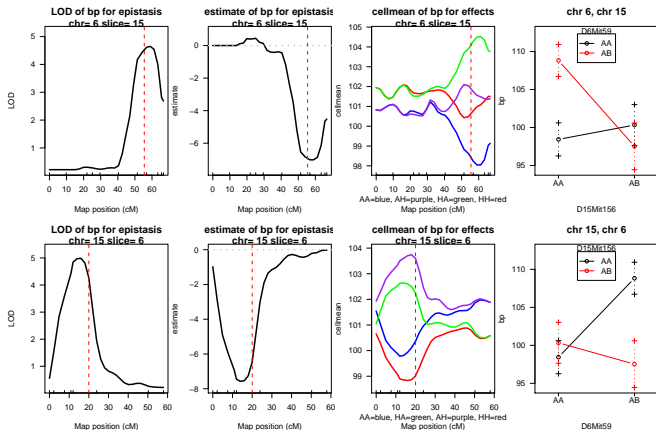
Epistatic Pair 1 and 7



Epistatic Pair 4 and 6



Epistatic Pair 6 and 15



final tasks:

remove objects created by R/bmqt1 if desired
externally run pdflatex twice on file hyperslide.tex

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