

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/Rinst62150217/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"

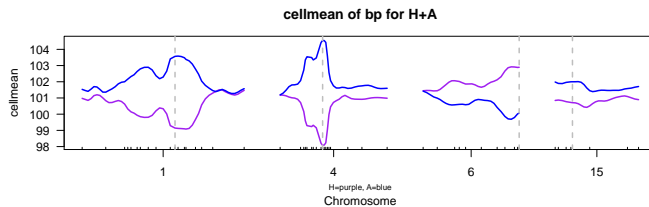
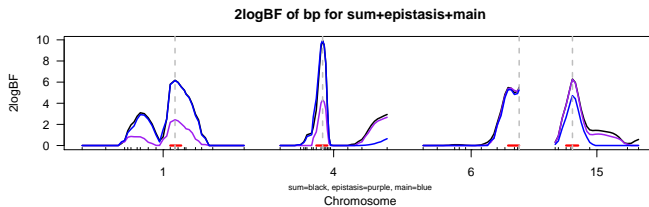
> cross.hpd <- qb.hpdone(cross.qb, hpd.level, scan.type)
> sum.one <- summary(cross.hpd)
> sum.one
```

	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	4029.5:4050	-0.1280	1.000
2	4029.5:4050	-0.1760	1.000
3	4029.5:4050	-0.1860	1.000
4	4029.5:4050	-0.1880	1.000
5	4029.5:4050	-0.0690	1.000
6	4029.5:4050	0.0536	0.630
7	6040.4:6062	-0.0172	1.000
8	4029.5:4050	0.0273	0.730
9	4050	-0.0491	1.000
10	15047.5	0.0557	0.620
11	6040.4	0.3440	0.217
12	4074.3	0.4920	0.139

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

	df	SS	MS	LOD	%var	Pvalue(Chi2)	Pvalue(F)
Model	6	6033.661	1005.61017	22.67922	34.14841	0	0
Error	243	11635.275	47.88179				
Total	249	17668.936					

Stepwise Reduction

	df	Type III SS	LOD	%var	F value	Pvalue(F)	
1@39.3	1	328.626	1.512	1.860	6.863	0.009352	**
1@71.3	1	552.503	2.518	3.127	11.539	0.000796	***
15@21.5	2	1365.270	6.023	7.727	14.257	1.40e-06	***
4@29.5	1	2808.662	11.739	15.896	58.658	4.44e-13	***
6@62	2	1561.571	6.837	8.838	16.307	2.26e-07	***
15@21.5:6@62	1	1091.999	4.870	6.180	22.806	3.10e-06	***

Reduced Genetic architecture

```
> cross.arch <- cross.step$aarch
> 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 by qtl, chr, pos:

	q1	q2	chra	chrb	posa	posb
pair	1	3	9	15	6	21.5 62.08

Epistatic chromosomes by connected sets:

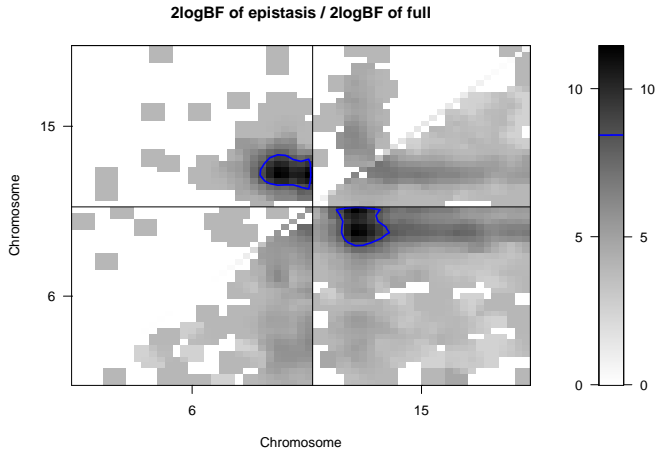
15,6

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

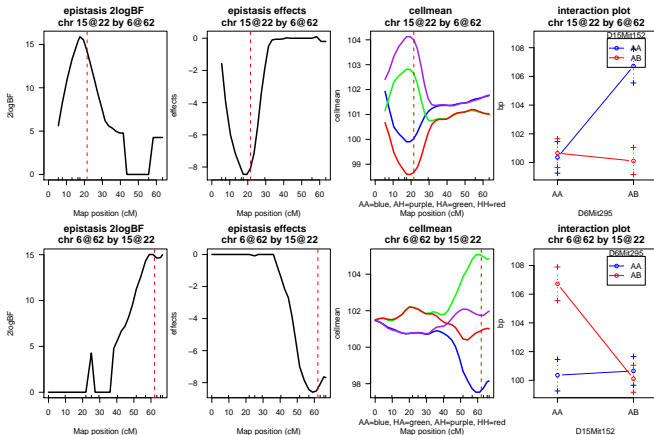


Slice Each Epistatic Pair

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

Epistatic Pair 15 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 .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)
+ }
```