

Prototype QTL Strategy: Phenotype SCD1 in Cross f2

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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(bmqt1)

> bmq.sweave(f2, pheno.col = 33,
+ n.iter = 3000, n.draws = 64,
+ threshold = c(main = 2, epistasis = 4, upper = 4),
+ maxpairs = c(20, 5),
+ SweaveFile = /u/y/a/yandell/public/statgen/R/bmqt1/doc/hyperslide.Rnw,
+ SweaveExtra = ,
+ PDFDir = SCD1PDF,
+ remove.bmq = FALSE)
```

Cross Object

```
> summary(cross)

F2 intercross

No. individuals: 512

No. phenotypes: 46
Percent phenotyped: 100 100 100 100 100 100 44.5 65.8 84.6 47.9 45.1 65 82.6 47.3 44.9 67.2 81.2 43.8

No. chromosomes: 19
Total markers: 290
No. markers: 22 25 14 18 18 12 16 12 15 14 14 12 19 12 13 16 14 10 14
Percent genotyped: 39
Genotypes (%): AA:24.9 AB:49.4 BB:25.7 not BB:0 not AA:0
```

Create MCMC runs

```
> cross <- bmq.genoprob(cross, step = 2, error = 0.01)

> cross.bmq <- bmq.mcmc(cross, genupdate=TRUE, n.iter = 3000,
+   verbose = FALSE)
```

1-D Bayes Factor Scan

```
> one <- bscanone(cross.bmq, type = "2logBF")  
> sum.one <- summary(one, threshold = threshold, sort = "sum")  
> sum.one
```

	chr	n.qtl	pos	e.pos	main	GxE	epistasis	sum
2	2	1.454	168.312	168.312	3.880	2.274	5.650	5.729
7	7	0.631	45.579	45.579	0.898	-0.026	4.879	4.900
9	9	1.072	57.803	30.305	4.283	-0.238	3.303	4.391
5	5	1.055	108.813	108.813	4.220	1.710	2.429	4.374

1-D Scan: Positions of Main QTL

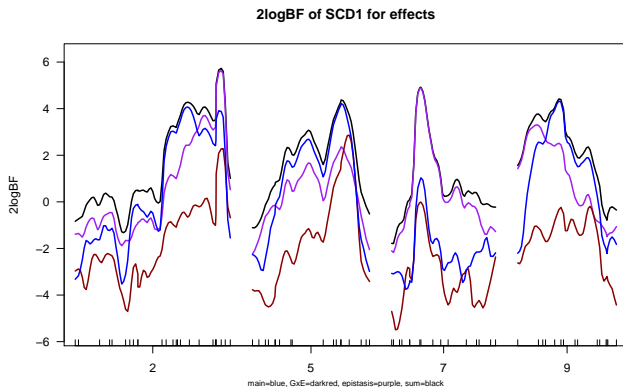
```
> chrs <- sort(as.vector(sum.one[, "chr"]))  
> pos <- sum.one[as.character(chrs), "pos"]  
> pos
```

```
      2      5      7      9  
168.312 108.813 45.579 57.803
```

plot key chromosomes on next slide

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

1-D Scan: BF 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	n.qtl	pos	A	H	B
2	2	1.454	168.312	1.626	1.809	1.969
5	5	1.055	108.813	1.296	1.887	2.209
9	9	1.072	57.803	2.331	1.814	1.284

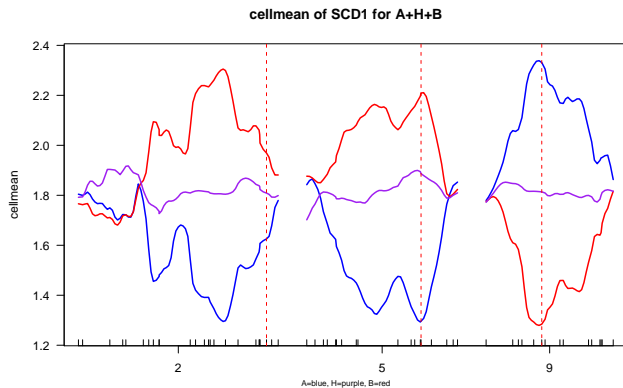
technical device to add vertical line at max BF:

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

	2	5	9
164.5086	299.7036	405.3056	

```
> 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 = "2logBF")  
> 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
2.7	2	7	0.975	168.312	45.579	6.418	168.312	45.579	6.384
2.9	2	9	1.571	168.312	19.712	5.327	168.312	19.712	5.282

Initial Genetic Architecture

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

```
      1      2      3      4      5
chr  2.00  5.00  7.00  9.00  9.0
pos 168.31 108.81 45.58 19.71 57.8
```

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

```
  1 2
q1 1 1
q2 3 4
```

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

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

```
  1 2
q1 2 2
q2 7 9
```

Construct QTL Object

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

```
> 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)
```

Stepwise Reduction

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

Stepwise Reduction

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

	df	SS	MS	LOD	%var	Pvalue(Chi2)	Pvalue(F)
Model	18	97.44672	5.4137069	21.25050	59.93231	5.447864e-13	4.727529e-11
Error	88	65.14792	0.7403173				
Total	106	162.59465					

Stepwise Reduction

	df	Type	III SS	LOD	%var	F value	Pvalue(F)	
Chr2@168.31	10		47.406	12.704	29.156	6.403	2.47e-07	***
Chr5@108.81	2		7.216	2.441	4.438	4.873	0.009835	**
Chr7@45.58	6		23.307	7.106	14.335	5.247	0.000116	***
Chr9@19.71	6		15.100	4.844	9.287	3.399	0.004605	**
Chr9@57.8	2		8.455	2.835	5.200	5.710	0.004659	**
Chr2@168.31:Chr7@45.58	4		21.053	6.506	12.948	7.109	5.24e-05	***
Chr2@168.31:Chr9@19.71	4		14.364	4.629	8.834	4.851	0.001395	**

Reduced Genetic architecture

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

      1      2      3      4      5
chr  2.00  5.00  7.00  9.00  9.0
pos 168.31 108.81 45.58 19.71 57.8

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

  1 2
q1 1 1
q2 3 4

above pairs index the qtl list
pairs below show chromosome pairs

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

  1 2
q1 2 2
q2 7 9
```

2-D Pairs

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

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

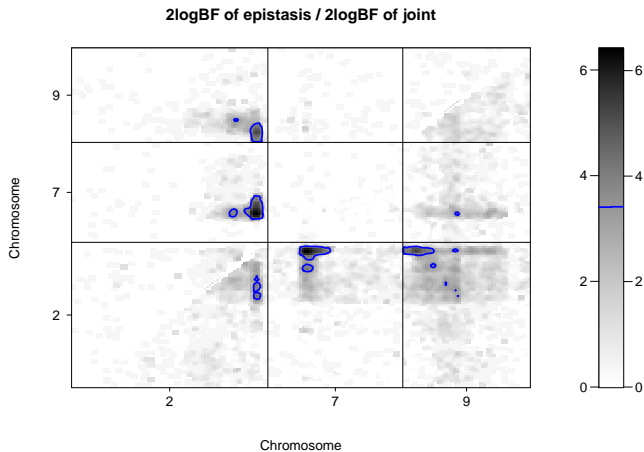
```
[[1]]  
[1] 2 7 9
```

2-D Plots

2-D plots by cliques (if any epistasis)

```
> 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

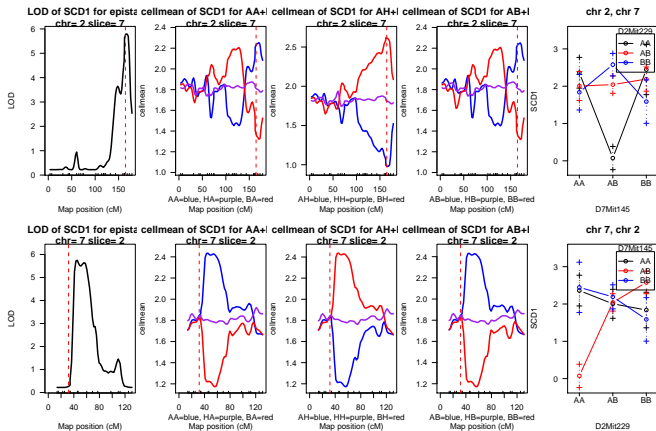


Slice Each Epistatic Pair

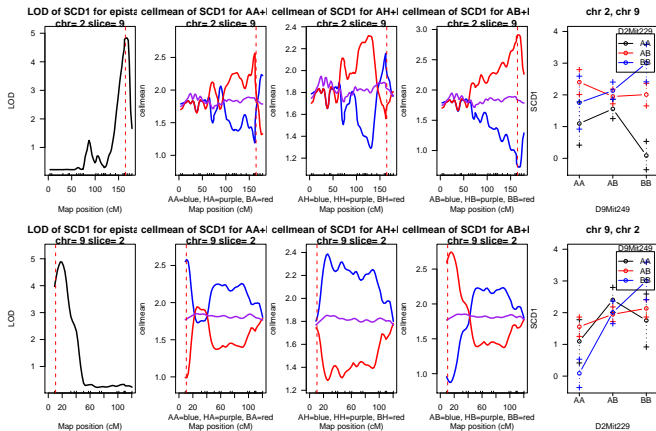
show detail plots for epistatic pairs (if any)

```
> 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 2 and 7



Epistatic Pair 2 and 9



final tasks:

clean cross object to reduce size

remove objects created by R/bmqtl if desired

externally run pdflatex twice on file hyperslide.tex

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