R/qtlbim (www.qtlbim.org)

- cross-compatible with R/qtl
- model selection for genetic architecture
  - epistasis, fixed & random covariates, GxE
  - samples multiple genetic architectures
  - examines summaries over nested models
- extensive graphics

R/qtlbim: tutorial

(www.stat.wisc.edu/~yandell/qtlbim)

```
> data(hyper)
## Drop X chromosome (for now).
> hyper <- subset(hyper, chr=1:19)
> hyper <- qb.genoprob(hyper, step=2)
## This is the time-consuming step:
> qbHyper <- qb.mcmc(hyper, pheno.col = 1)
## Here we get stored samples.
> qb.load(hyper, qbHyper)
> summary(qbHyper)
```

R/qtlbim: initial summaries

```
> summary(qbHyper)

Bayesian model selection QTL mapping object qbHyper on cross object hyper
had 3000 iterations recorded at each 40 steps with 1200 burn-in steps.

Diagnostic summaries:
           nqtl   mean envvar varadd  varaa    var
Min.      2.000  97.42  28.07  5.112  0.000  5.112
1st Qu.   5.000 101.00  44.33 17.010  1.639 20.180
Median    7.000 101.30  48.57 20.060  4.580 25.160
Mean      6.543 101.30  48.80 20.310  5.321 25.630
3rd Qu.   8.000 101.70  53.11 23.480  7.862 30.370
Max.     13.000 103.90  74.03 51.730 34.940 65.220

Percentages for number of QTL detected:
 2  3  4  5  6  7  8  9 10 11 12 13
 2  3  9 14 21 19 17 10  4  1  0  0

Percentages for number of epistatic pairs detected:
pairs
 1  2  3  4  5  6
29 31 23 11  5  1

Percentages for common epistatic pairs:
 6.15  4.15   4.6   1.7 15.15   1.4   1.6   4.9  1.15  1.17   1.5  5.11   1.2  7.15   1.1
   63    18    10     6     6     5     4     4     3     3     3     2     2     2     2

> plot(qb.diag(qbHyper, items = c("herit", "envvar")))
```

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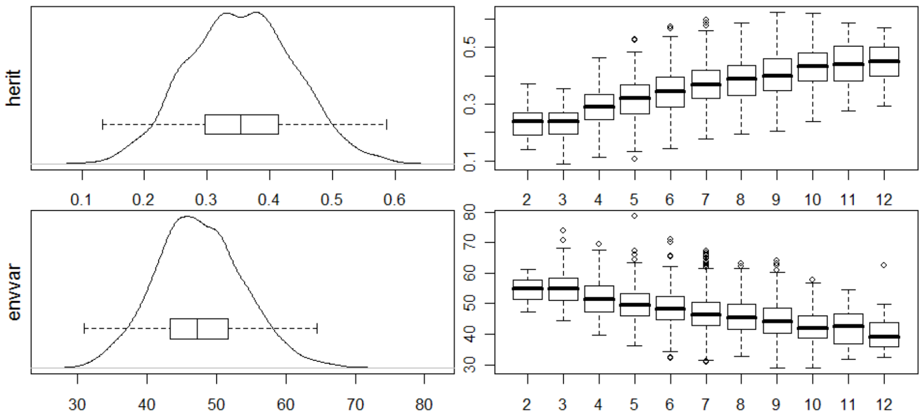
diagnostic summaries



R/qtlbim: 1-D (*not* 1-QTL!) scan

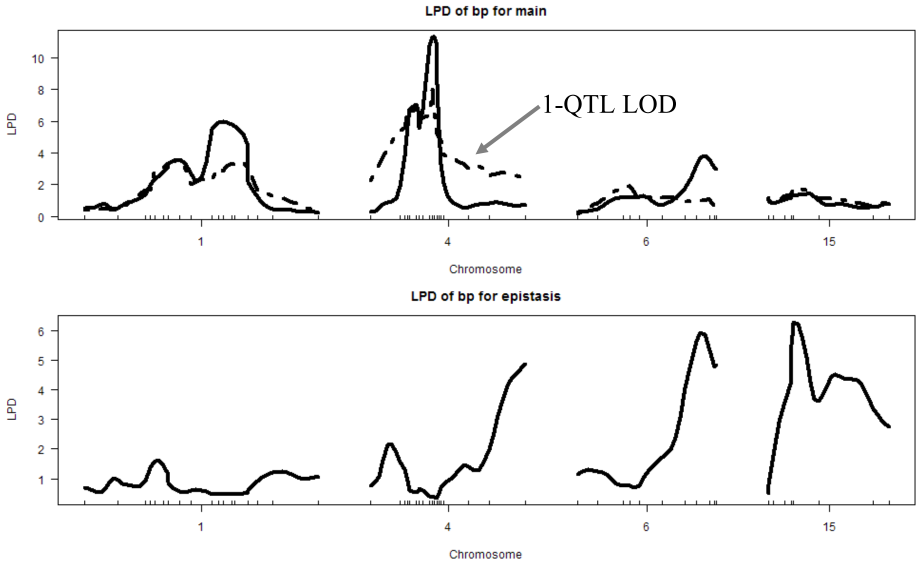
```
> one <- qb.scanone(qbHyper, chr = c(1,4,6,15), type =
   "LPD")
> summary(one)

LPD of bp for main,epistasis,sum

    n.qtl  pos m.pos e.pos  main epistasis   sum
c1  1.331 64.5  64.5  67.8  6.10     0.442  6.27
c4  1.377 29.5  29.5  29.5 11.49     0.375 11.61
c6  0.838 59.0  59.0  59.0  3.99     6.265  9.60
c15 0.961 17.5  17.5  17.5  1.30     6.325  7.28

> plot(one, scan = "main")
> plot(out.em, chr=c(1,4,6,15), add = TRUE, lty = 2)
> plot(one, scan = "epistasis")
```

1-QTL LOD vs. marginal LPD


LPD of bp for main

1-QTL LOD

LPD of bp for epistasis

most probable patterns

```
> summary(qb.BayesFactor(qbHyper, item = "pattern"))

                  nqtl posterior    prior    bf  bfse
1,4,6,15,6:15        5   0.03400 2.71e-05 24.30 2.360
1,4,6,6,15,6:15      6   0.00467 5.22e-06 17.40 4.630
1,1,4,6,15,6:15      6   0.00600 9.05e-06 12.80 3.020
1,1,4,5,6,15,6:15    7   0.00267 4.11e-06 12.60 4.450
1,4,6,15,15,6:15     6   0.00300 4.96e-06 11.70 3.910
1,4,4,6,15,6:15      6   0.00300 5.81e-06 10.00 3.330
1,2,4,6,15,6:15      6   0.00767 1.54e-05  9.66 2.010
1,4,5,6,15,6:15      6   0.00500 1.28e-05  7.56 1.950
1,2,4,5,6,15,6:15    7   0.00267 6.98e-06  7.41 2.620
1,4                  2   0.01430 1.51e-04  1.84 0.279
1,1,2,4              4   0.00300 3.66e-05  1.59 0.529
1,2,4                3   0.00733 1.03e-04  1.38 0.294
1,1,4                3   0.00400 6.05e-05  1.28 0.370
1,4,19               3   0.00300 5.82e-05  1.00 0.333

> plot(qb.BayesFactor(qbHyper, item = "nqtl"))
```

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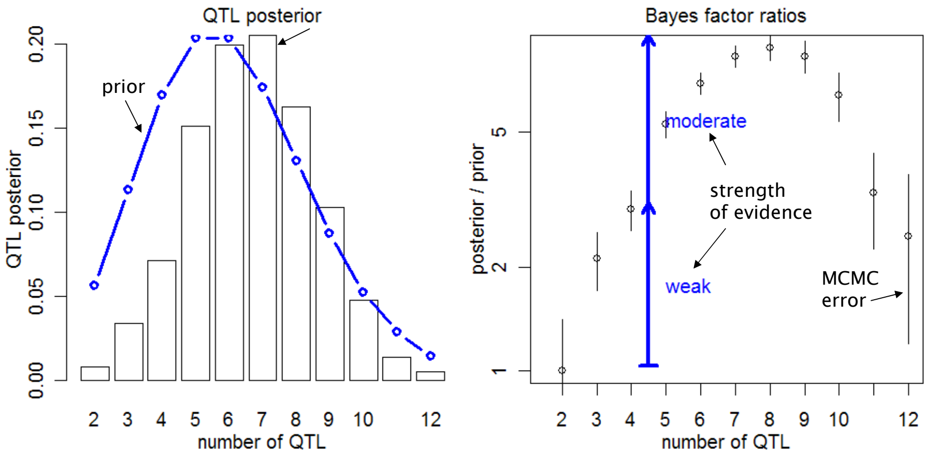
hyper: number of QTL posterior, prior, Bayes factors



what is best estimate of QTL?

- find most probable pattern
  - 1,4,6,15,6:15 has posterior of 3.4%
- estimate locus across all nested patterns
  - Exact pattern seen ~100/3000 samples
  - Nested pattern seen ~2000/3000 samples
- estimate 95% confidence interval using quantiles

```
> best <- qb.best(qbHyper)
> summary(best)$best

    chrom locus locus.LCL locus.UCL     n.qtl
247     1  69.9  24.44875   95.7985 0.8026667
245     4  29.5  14.20000   74.3000 0.8800000
248     6  59.0  13.83333   66.7000 0.7096667
246    15  19.5  13.10000   55.7000 0.8450000

> plot(best)
```

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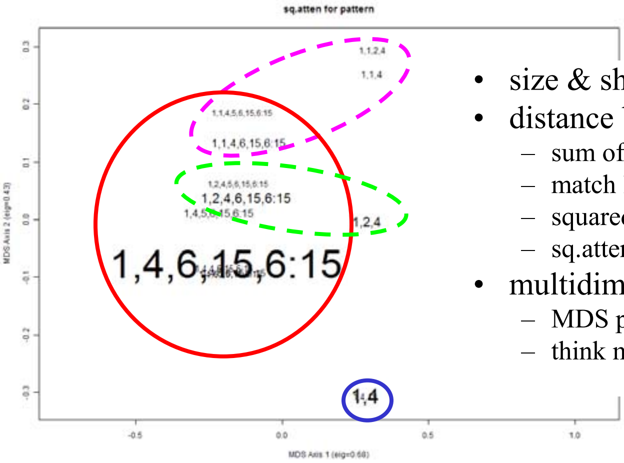
what patterns are “near” the best?



- size & shade ~ posterior
- distance between patterns
  - sum of squared attenuation
  - match loci between patterns
  - squared attenuation = $(1-2r)^2$
  - sq.atten in scale of LOD & LPD
- multidimensional scaling
  - MDS projects distance onto 2-D
  - think mileage between cities

how close are other patterns?

```
> target <- qb.best(qbHyper)$model[[1]]
> summary(qb.close(qbHyper, target))

 score by sample number of qtl
    Min. 1st Qu. Median  Mean 3rd Qu.  Max.
2  1.437   1.735  1.919 1.834   1.919 2.000
3  1.351   1.735  1.916 1.900   1.919 2.916
4  1.270   1.916  2.437 2.648   3.574 4.000
5  1.295   1.919  2.835 2.798   3.611 4.000
6  1.257   2.254  3.451 3.029   3.648 4.000
...
13 3.694   3.694  3.694 3.694   3.694 3.694

 score by sample chromosome pattern
                    Percent  Min. 1st Qu. Median  Mean 3rd Qu.  Max.
4@1,4,6,15,6:15         3.4 2.946   3.500  3.630 3.613   3.758 4.000
2@1,4                   1.4 1.437   1.735  1.919 1.832   1.919 2.000
5@1,2,4,6,15,6:15       0.8 3.137   3.536  3.622 3.611   3.777 3.923
3@1,2,4                 0.7 1.351   1.700  1.821 1.808   1.919 2.000
5@1,1,4,6,15,6:15       0.6 3.257   3.484  3.563 3.575   3.698 3.916
5@1,4,5,6,15,6:15       0.5 3.237   3.515  3.595 3.622   3.777 3.923
5@1,4,6,6,15,6:15       0.5 3.203   3.541  3.646 3.631   3.757 3.835
...

> plot(close)
> plot(close, category = "nqtl")
```

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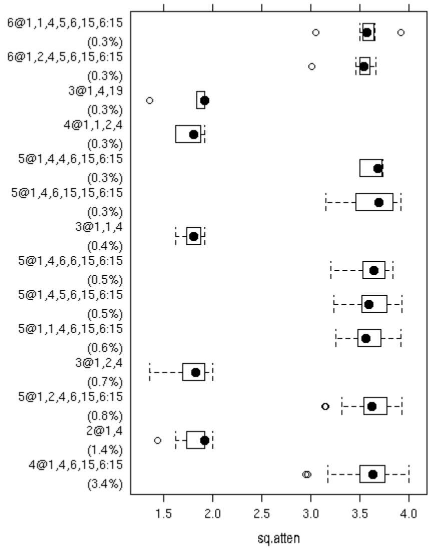
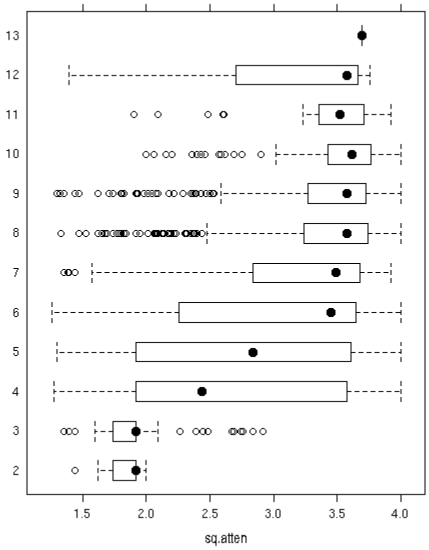
how close are other patterns?

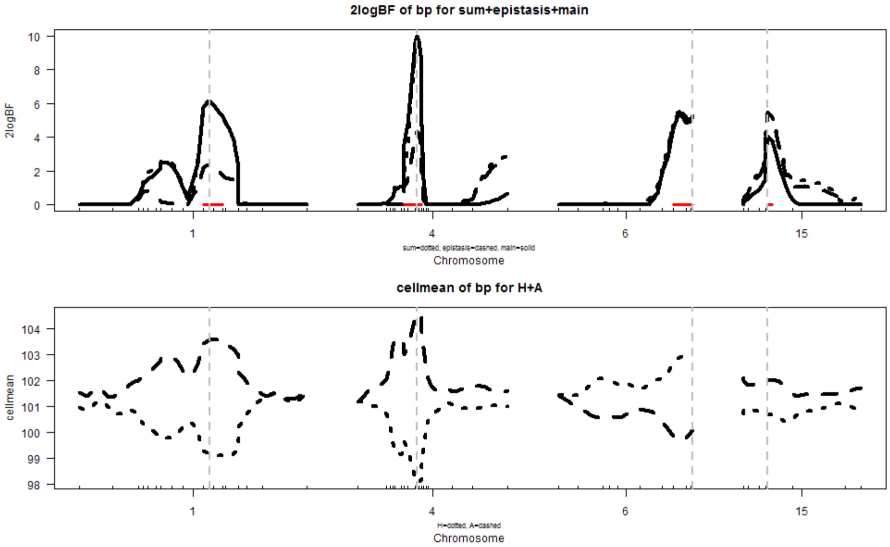




R/qtlbim: automated QTL selection

```
> hpd <- qb.hpdone(qbHyper, profile = "2logBF")
> summary(hpd)

   chr n.qtl  pos lo.50% hi.50% 2logBF       A       H
1    1 0.829 64.5   64.5   72.1  6.692 103.611  99.090
4    4 3.228 29.5   25.1   31.7 11.169 104.584  98.020
6    6 1.033 59.0   56.8   66.7  6.054  99.637 102.965
15  15 0.159 17.5   17.5   17.5  5.837 101.972 100.702

> plot(hpd)
```

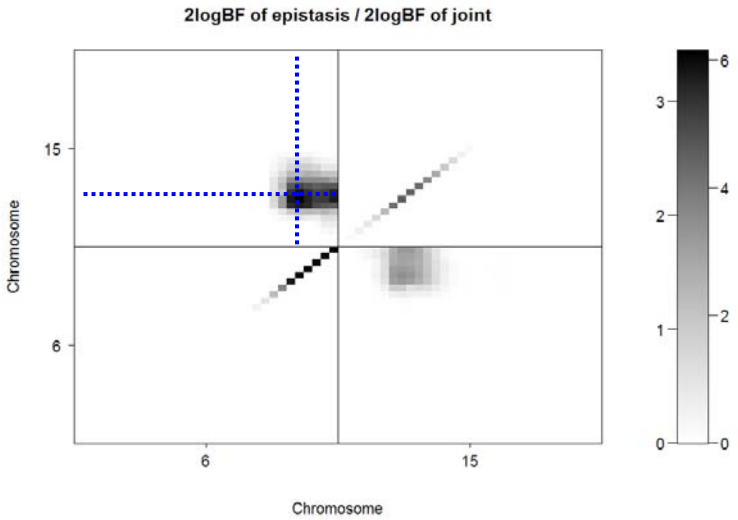
2log(BF) scan with 50% HPD region



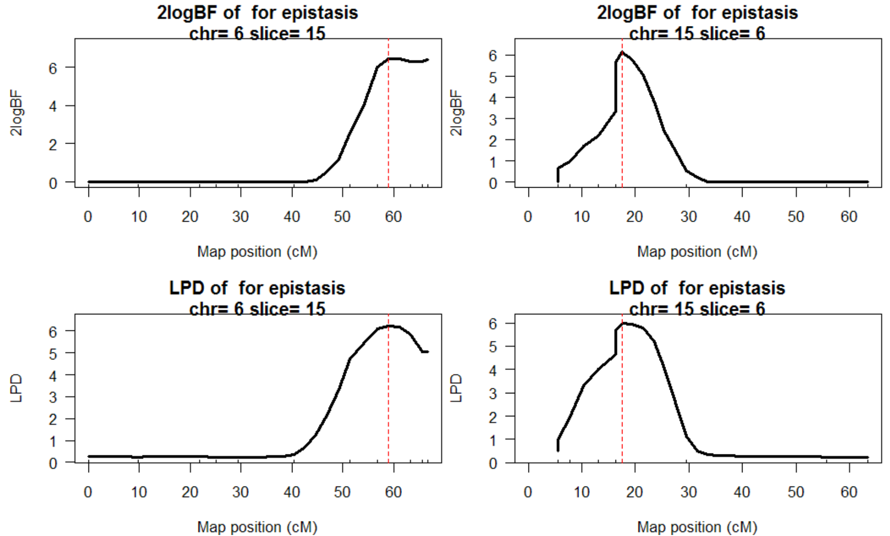
R/qtlbim: 2-D (*not* 2-QTL) scans

```
> two <- qb.scantwo(qbHyper, chr = c(6,15),
  type = "2logBF")
> plot(two)

> plot(two, chr = 6, slice = 15)
> plot(two, chr = 15, slice = 6)

> two.lpd <- qb.scantwo(qbHyper, chr = c(6,15),
  type = "LPD")
> plot(two.lpd, chr = 6, slice = 15)
> plot(two.lpd, chr = 15, slice = 6)
```

2-D plot of 2logBF: chr 6 & 15

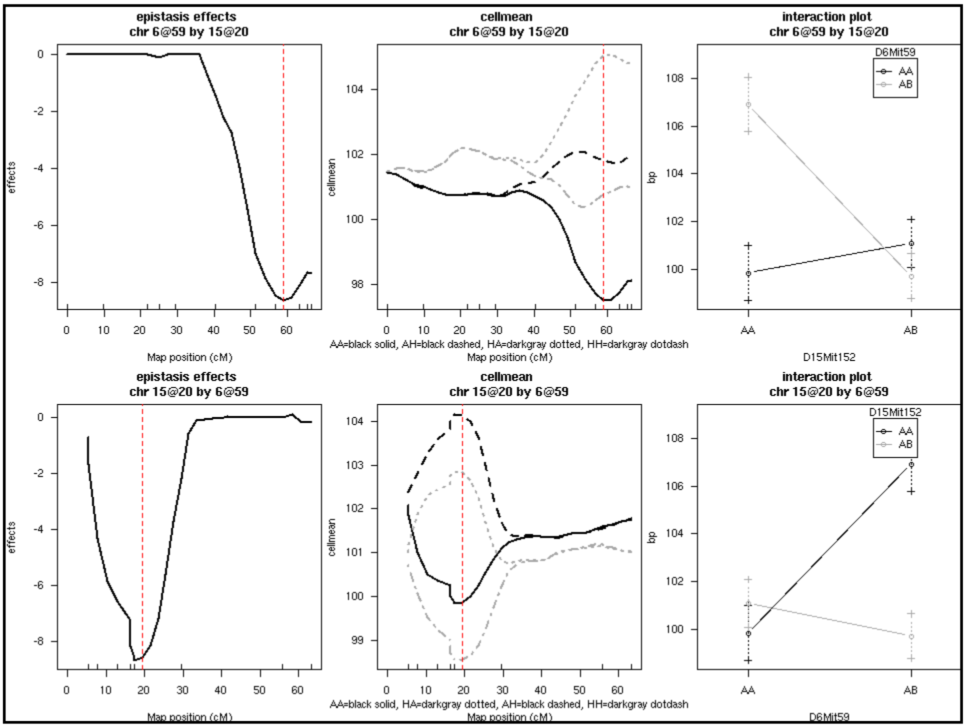


1-D Slices of 2-D scans: chr 6 & 15



R/qtlbim: slice of epistasis

```
> slice <- qb.slicetwo(qbHyper, c(6,15), c(59,19.5))
> summary(slice)

2logBF of bp for epistasis

    n.qtl  pos m.pos e.pos epistasis slice
c6  0.838 59.0  59.0  66.7      15.8  18.1
c15 0.961 17.5  17.5  17.5      15.5  60.6

cellmean of bp for AA,HA,AH,HH

    n.qtl  pos m.pos   AA  HA  AH    HH slice
c6  0.838 59.0  59.0 97.4 105 102 100.8  18.1
c15 0.961 17.5  17.5 99.8 103 104  98.5  60.6

estimate of bp for epistasis

    n.qtl  pos m.pos e.pos epistasis slice
c6  0.838 59.0  59.0  66.7     -7.86  18.1
c15 0.961 17.5  17.5  17.5     -8.72  60.6

> plot(slice, figs = c("effects", "cellmean", "effectplot"))
```



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selected publications

www.stat.wisc.edu/~yandell/statgen

- www.qtlbim.org
- vignettes in R/qtlbim package
- Yandell, Bradbury (2007) *Plant Map* book chapter
  - overview/comparison of QTL methods
- Yandell et al. (2007 *Bioinformatics*)
  - R/qtlbim introduction
- Yi et al. (2005 *Genetics,* 2007 *Genetics*)
  - methodology of R/qtlbim