

Bayesian Interval Mapping

Brian S. Yandell, Patrick J. Gaffney, Jaya M. Satagopan, Chunfang Jin and Hao Wu

October 6, 2003

1 Overview

Bayesian interval mapping library R/bim provides Bayesian analysis of multiple quantitative trait loci (QTL) models. This includes posterior estimates of the number and location of QTL, and of their effects. This document assumes some familiarity with QTL and with Bayesian methods. In addition it provides graphical diagnostics that can help investigate several ‘better’ models. Library R/bim requires R/qlt and R/modreg.

```
> library(bim)
```

Loading required package: qlt

2 Bayesian Interval Mapping

Consider a simple problem, the 8-week vernalization data for *Brassica napus* used by Satagopan et al (1996).

```
> data(vern)
```

```
> summary(vern)
```

Backcross

No. individuals: 104

No. phenotypes: 1

Percent phenotyped: 100

No. chromosomes: 1

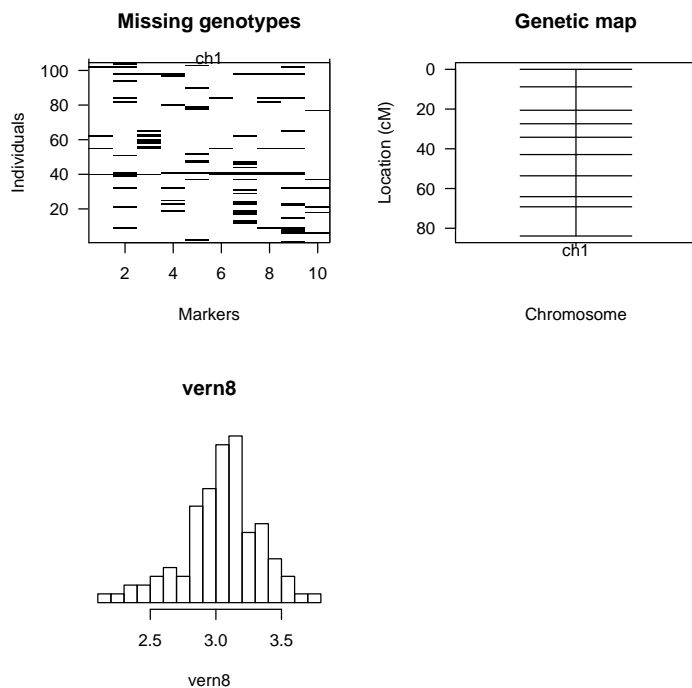
Total markers: 10

No. markers: 10

Percent genotyped: 90.9

Genotypes (%): AA:41.4 AB:58.6

```
> plot(vern)
```



These data are treated as a backcross (although in fact they are from a double haploid, homozygous at every locus). The plot, from library R/qtl, shows the pattern of missing genotypes, the linkage map, and the 11 traits. We focus on `log10flower8`, the logarithm base 10 of the flowering time after eight weeks of vernalization.

Bayesian interval mapping proceeds by first running the `bmapqtl` Markov chain Monte Carlo simulation of the posterior.

```
> bmapqtl.options(prior.nqtl = "poisson")
```

```
simulate 400000 MCMC steps, recording by 400 with 0.05 burnin and 0.05 pre-burnin
prior for number of QTL: poisson(3)
initial number of QTL: 0
hyperparameters for priors:
      1  2
init    0.5 -1
prior.mean 1.0 -1
prior.var  3.0 -1
prior.add  0.0  0
prior.dom  0.0  0
random seed: 0
```

```
> vernpois.bim = run.bmapqtl(vern)
```

Bayesian interval mapping MCMC run in progress.

Count of 1000 iterations shown separated by dots (negative for burnin):

```
-20.-15.-10.-5.0.
```

```
5.10.15.20.25.30.35.40.45.50.
```

```
55.60.65.70.75.80.85.90.95.100.
```

```
105.110.115.120.125.130.135.140.145.150.
```

```
155.160.165.170.175.180.185.190.195.200.
```

```
205.210.215.220.225.230.235.240.245.250.
```

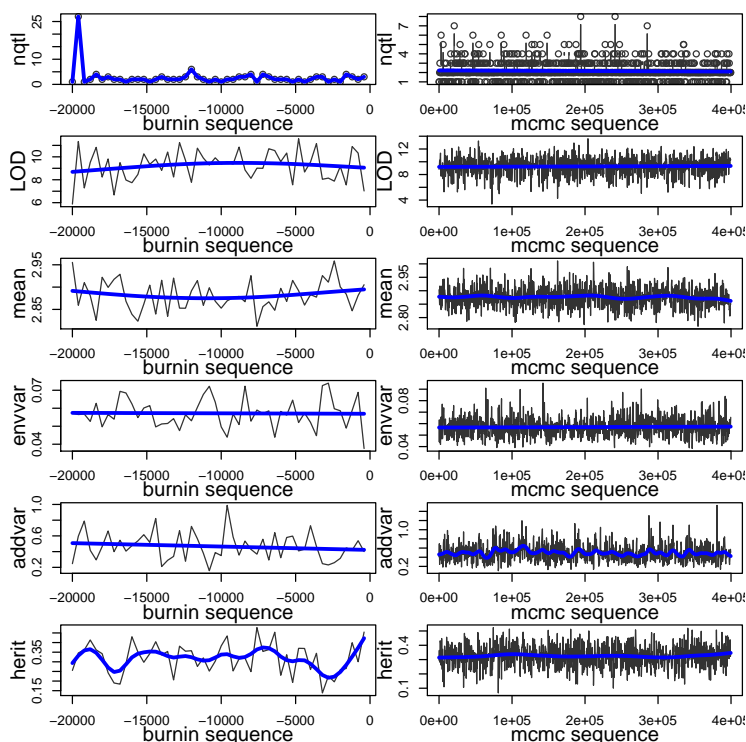
```
255.260.265.270.275.280.285.290.295.300.
```

```
305.310.315.320.325.330.335.340.345.350.
```

```
355.360.365.370.375.380.385.390.395.
```

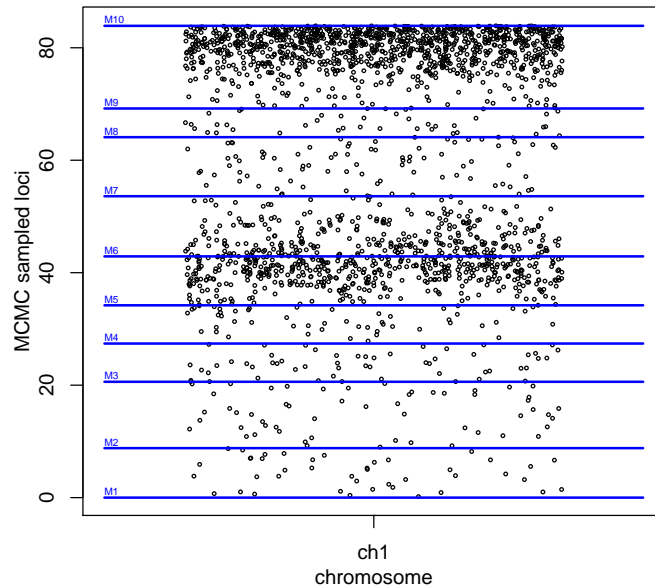
Now that we have the MCMC simulations, we can examine diagnostic plots. First, time series of the burnin and MCMC runs gives a graphical idea of how well the simulations are ‘mixing’.

```
> plot.bim.mcmc(vernpois.bim)
```



A jittered plot of quantitative trait loci by chromosome shows the where the posterior concentrates along the genome relative to the marker map.

```
> plot.bim.loci(vernpois.bim, vern)
```



Model selection is assisted by four plots. The top two concern the number of QTL while the bottom two are for the pattern of loci across chromosomes. The left panel shows the posterior as a histogram, overlaid by the prior (rescaled to fit). The right panel show the posterior to prior ratios which make up Bayes factors. A large vertical separation on a log scale indicates substantial difference among models. The summary shows in numbers what is found in the plots.

```
> model = bim.model(vernpois.bim, vern)
> summary(model)

posterior for number of QTL as %
  1  2  3  4  5  6  7  8
22 52 17  6  2  0  0  0
Bayes factor ratios for number of QTL
  1  2  3  4  5  6  7  8
1.0 1.6 0.5 0.2 0.1 0.1 0.1 0.2
model posterior above cutoff 1 as %
2*1  1 3*1 4*1 5*1
 52 22 17  6  2
Bayes factor ratios for chromosome pattern
2*1  1 3*1 4*1 5*1
1.0 1.3 0.2 0.1 0.0

> plot(model)
```

\$nctl
\$nctl\$posterior

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|-------|-------|-------|-------|-------|-------|-------|-------|
| 0.222 | 0.519 | 0.172 | 0.062 | 0.016 | 0.005 | 0.002 | 0.002 |

\$nctl\$prior

| 1 | 2 | 3 | 4 | 5 | 6 |
|-------------|-------------|-------------|-------------|-------------|-------------|
| 0.149361205 | 0.224041808 | 0.224041808 | 0.168031356 | 0.100818813 | 0.050409407 |
| 7 | 8 | | | | |
| 0.021604031 | 0.008101512 | | | | |

\$nctl\$bf

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|------------|------------|------------|------------|------------|------------|------------|
| 1.00000000 | 1.55855856 | 0.51651652 | 0.24824825 | 0.10677344 | 0.06673340 | 0.06228451 |
| 8 | | | | | | |
| 0.16609202 | | | | | | |

\$nctl\$bfse

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|------------|------------|------------|------------|------------|------------|------------|
| 0.05919886 | 0.04744735 | 0.03583729 | 0.03053457 | 0.02647895 | 0.02976938 | 0.04399773 |
| 8 | | | | | | |
| 0.11732729 | | | | | | |

\$pattern
\$pattern\$posterior

| 2*1 | 1 | 3*1 | 4*1 | 5*1 |
|-------|-------|-------|-------|-------|
| 0.519 | 0.222 | 0.172 | 0.062 | 0.016 |

\$pattern\$prior

| 2*1 | 1 | 3*1 | 4*1 | 5*1 |
|------------|------------|------------|------------|------------|
| 0.14936121 | 0.04978707 | 0.22404181 | 0.22404181 | 0.16803136 |

\$pattern\$bf

| 2*1 | 1 | 3*1 | 4*1 | 5*1 |
|------------|------------|------------|------------|------------|
| 1.00000000 | 1.28323699 | 0.22093770 | 0.07964033 | 0.02740313 |

\$pattern\$bfse

| 2*1 | 1 | 3*1 | 4*1 | 5*1 |
|-------------|-------------|-------------|-------------|-------------|
| 0.030443099 | 0.075966162 | 0.015329245 | 0.009795772 | 0.006795754 |

\$param

```

$param$nqtl
[1] 1

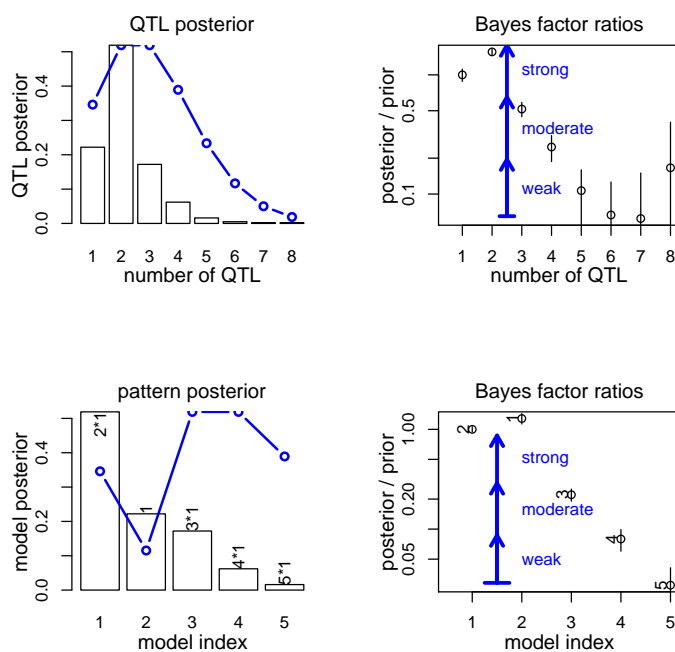
$param$pattern
NULL

$param$exact
[1] FALSE

$param$cutoff
[1] 1

attr(,"class")
[1] "bim.model"

```



The effects plots show the quantitative trait loci by a histogram and density (blue) on the top plot and effects (additive and possibly dominance) in scatter plot with a smoothing spline fit plus or minus two standard errors. Vertical lines (red) identify the estimated QTL. The summary shows the estimated QTL loci and effects.

```

> qtl = plot.bim.effects(vernpois.bim, vern)
> summary(qtl)

```

QTL loci and density peaks:

| chr | loci | dens |
|-----|--------------|-----------|
| 1 | ch1 81.28166 | 0.0579028 |

HPD region density cutoffs:

| 0.5 | 0.55 | 0.6 | 0.65 | 0.7 | 0.75 |
|-------------|-------------|-------------|-------------|-------------|-------------|
| 0.027622297 | 0.025171976 | 0.022465807 | 0.019018241 | 0.015372926 | 0.011697632 |
| 0.8 | 0.85 | 0.9 | 0.95 | | |
| 0.007841648 | 0.004631643 | 0.003782281 | 0.002930640 | | |

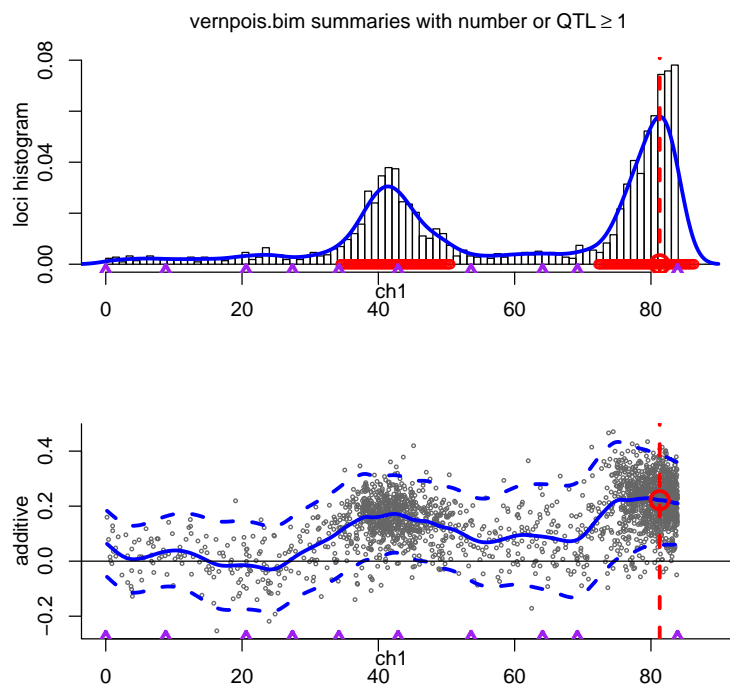
QTL loci and effect estimates:

| chrom | loci | add | add.sd |
|-------|--------------|--------------|------------|
| ch1 | ch1 81.28166 | 0.2217985 | 0.08198312 |
| | mean | NA 2.8760781 | 0.03777311 |

QTL density estimates by chromosome at 512 grid points with bw = 2

Smoothing spline parameters for additive effects:

ch1
0.9004665

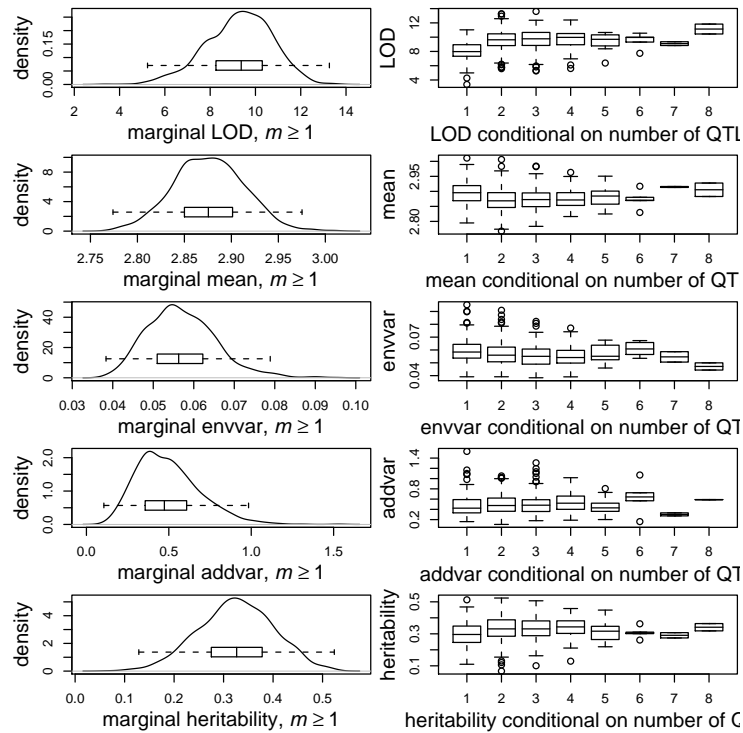


Finally, summary diagnostics for model parameters are shown as histograms and boxplots conditional on the number of QTL. Notice how the boxplots level

out as the model gets more complex, although there is very little data for models with a large number of QTL.

```
> plot.bim.diag(vernpois.bim)
```

```
LOD 9.372
conditional LOD
      1      2      3      4      5      6      7      8
7.978 9.633 9.771 9.971 9.699 9.961 9.096 11.138
mean 2.876
conditional mean
      1      2      3      4      5      6      7      8
2.896 2.869 2.873 2.871 2.884 2.870 2.915 2.905
envvar 0.056
conditional envvar
      1      2      3      4      5      6      7      8
0.058 0.056 0.055 0.054 0.055 0.061 0.055 0.047
addvar 0.473
conditional addvar
      1      2      3      4      5      6      7      8
0.423 0.475 0.481 0.520 0.429 0.642 0.302 0.590
herit 0.326
conditional heritability
      1      2      3      4      5      6      7      8
0.296 0.331 0.331 0.343 0.316 0.306 0.291 0.341
```

All of these plots can be produced by one call to `plot(vernpois.bim,vern)`. Following this initial investigation, we can refine our graphics by restricting attention to ‘better’ models. For instance, the model selection suggests two QTL on the chromosome. The option `pattern` can pick up only those simulations that have 2 QTL on this chromosome. We can then reexamine the model

```
> plot.bim.model(vernpois.bim, vern, pattern = c(1, 1))

$nqtl
$nqtl$posterior
      2      3      4      5      6      7
0.667095116 0.221079692 0.079691517 0.020565553 0.006426735 0.002570694
      8
0.002570694

$nqtl$prior
      2      3      4      5      6      7
0.224041808 0.224041808 0.168031356 0.100818813 0.050409407 0.021604031
      8
0.008101512

$nqtl$bf
```

| | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|--|------------|------------|------------|------------|------------|------------|------------|
| | 1.00000000 | 0.33140655 | 0.15928067 | 0.06850781 | 0.04281738 | 0.03996289 | 0.10656771 |

\$nqtl\$bfse

| | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|--|------------|------------|------------|------------|------------|------------|------------|
| | 0.02532657 | 0.02230198 | 0.01940591 | 0.01694993 | 0.01908689 | 0.02822169 | 0.07525783 |

\$pattern

\$pattern\$posterior

| | 2*1 | 3*1 | 4*1 | 5*1 |
|--|------------|------------|------------|------------|
| | 0.66709512 | 0.22107969 | 0.07969152 | 0.02056555 |

\$pattern\$prior

| | 2*1 | 3*1 | 4*1 | 5*1 |
|--|-----------|-----------|-----------|-----------|
| | 0.1493612 | 0.2240418 | 0.2240418 | 0.1680314 |

\$pattern\$bf

| | 2*1 | 3*1 | 4*1 | 5*1 |
|--|------------|------------|------------|------------|
| | 1.00000000 | 0.22093770 | 0.07964033 | 0.02740313 |

\$pattern\$bfse

| | 2*1 | 3*1 | 4*1 | 5*1 |
|--|-------------|-------------|-------------|-------------|
| | 0.025326572 | 0.014867985 | 0.009702953 | 0.006779970 |

\$param

\$param\$nqtl

[1] 1

\$param\$pattern

[1] 1 1

\$param\$exact

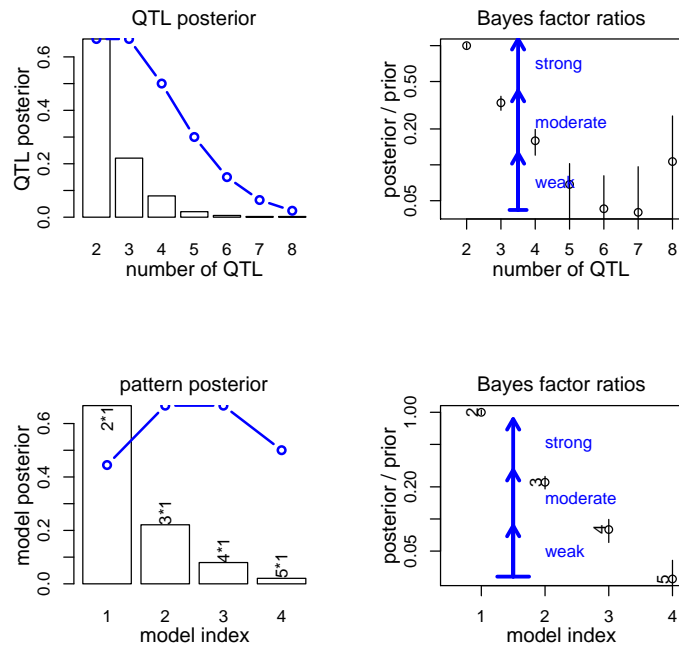
[1] FALSE

\$param\$cutoff

[1] 1

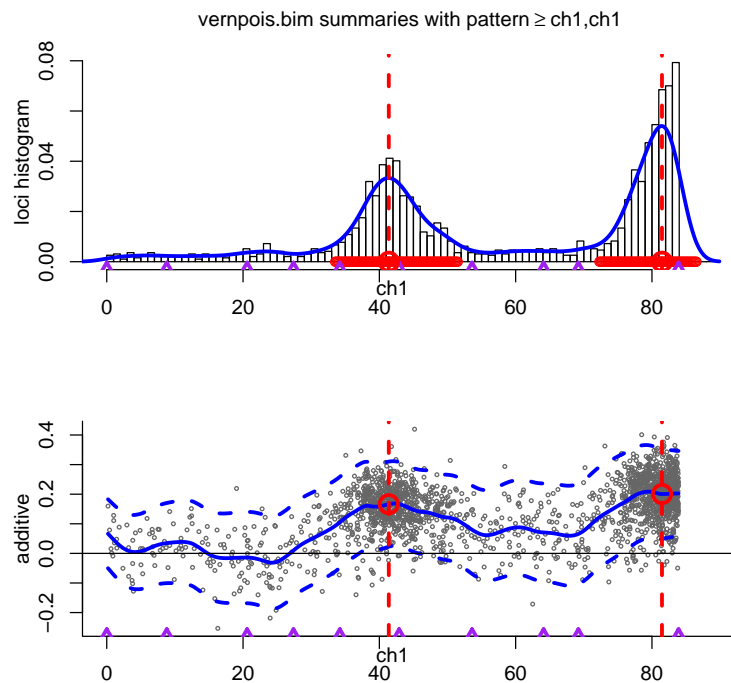
attr(,"class")

[1] "bim.model"



and reexamine the effects

```
> plot.bim.effects(vernpois.bim, vern, pattern = c(1, 1))
```



This subsetting is even more effective for full-genome studies. Consider analyzing the full **Bnapus** dataset for the trait `log10flower8`.

We can assess the false discovery rate, which gives us some feedback on the width of highest probability density (HPD) regions for QTLs (horizontal red lines on loci histograms).

```
> plot.bim.fdr(vernpois.bim, vern, pattern = c(1, 1))
```

```
      H0      M0      M1
0.2353702 0.0000000 1.0000000
```

```
$hyp
```

```
      H0      M0      M1
0.235 0.000 1.000
```

```
$fdr
```

```
0.05 0.1 0.15 0.2 0.25
0.19 0.74 0.87 0.95 0.99
```

