VISG Virtual Institute of Statistical Genetics

Bayesian QTL mapping for allo-polyploids and diploids with BayesQTLBIC.

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Part I: Peeling for allo-polyploids (and diploids)

Strategy: peeling $\longrightarrow$ Bayesian QTL mapping

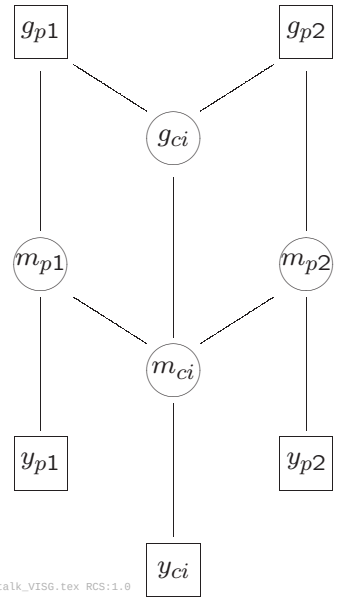
Software: R packages `polyploids` and `BayesQTLBIC`

Peeling

Elston & Stewart 1971.

- method for evaluating probability distribution on a pedigree
- Bayesian graphical model
- utilises conditional independence in graphical model, avoids calculating all possible combinations (often impossibly many)

Polyploids peeling graphical model



Peeling—a rough idea

1. sum over possibilities for a node; 'peel' it away $\rightsquigarrow$ structure on reduced graph ('$R()$' functions on parent nodes).

2. repeat to peel down to single mode (or nothing) $\longrightarrow$ marginal probability (or likelihood)

3. for sampling, reverse the process

Peeling equations

Note the $R_{gci}(\cdot)$ etc functions, don't worry too much about the details.

The joint distribution is:

$$f(m_{p_1}, m_{p_2}, \ldots) = [m_{p_1}][m_{p_2}][y_{p_1} \mid m_{p_1}][y_{p_2} \mid m_{p_2}] \times \prod_{i=1}^{n} [g_{c_i} \mid g_{p_1}, g_{p_2}][m_{c_i} \mid m_{p_1}, m_{p_2}, g_{c_i}][y_{c_i} \mid m_{c_i}] \quad (1)$$

Let:

$$\begin{aligned} R_{gci}(g_{c_i}, m_{p_1}, m_{p_2}) &= \sum_{m_{c_i}} [m_{c_i} \mid m_{p_1}, m_{p_2}, g_{c_i}][y_{c_i} \mid m_{c_i}] \\ &= I(f_2(f_1(m_{p_1}, m_{p_2}, g_{c_i})) = y_{ci}) \quad (2) \end{aligned}$$

The joint distribution after 'peeling' progeny marker genotypes m_{ci} becomes:

$$f(m_{p_1}, m_{p_2}, g_{c_1}, g_{c_2}, \ldots) = [m_{p_1}][m_{p_2}][y_{p_1} \mid m_{p_1}][y_{p_2} \mid m_{p_2}] \times \prod_{i=1}^{n} [g_{c_i} \mid g_{p_1}, g_{p_2}] R_{gci}(g_{c_i}, m_{p_1}, m_{p_2}) \quad (3)$$

Next peel g_{c_i}:

$$R_{gp1p2i}(g_{p1}, g_{p2}, m_{p1}, m_{p2}) = \sum_{g_{ci}} [g_{ci} | g_{p1}, g_{p2}] R_{gci}(g_{ci}, m_{p1}, m_{p2}) \quad (4)$$

For allo-tetraploids we obtain:

$$R_{gp1p2i}(g_{p1}, g_{p2}, m_{p1}, m_{p2}) = \sum_{g_{ci}} \frac{1}{2^4} I(g_{ci} \in c(1|2,5|6,3|4,7|8)) \times R_{gci}(g_{ci}, m_{p1}, m_{p2}) \quad (5)$$

where the notation $1|2, 5|6, \ldots$ means 1 or 2 and 5 or 6 etc. For allo-polyploids with ploidy $2k$ we have a similar expression with the factor $\frac{1}{2^4}$ is replaced by $\frac{1}{2^{2k}}$ in (5).

$$f(m_{p1}, m_{p2}) = [m_{p1}][m_{p2}][y_{p1}|m_{p1}][y_{p2}|m_{p2}] \times \prod_{i=1}^{n} R_{gp1p2i}(g_{p1}, g_{p2}, m_{p1}, m_{p2}) \quad (6)$$

Finally peel m_{p2}:

$$R_{mp1}(m_{p1}) = \sum_{m_{p2}} [m_{p2}] I(f_2(m_{p2}) = y_{p2}) R_{gp1p2i}(g_{p1}, g_{p2}, m_{p1}, m_{p2}) \quad (7)$$

$$f(m_{p1}) = [m_{p1}][y_{p1}|m_{p1}] R_{mp1}(m_{p1}) \quad (8)$$

Peeling—small example

Blood example (fictitious).
Diploid: 12 × 34

- 6 markers, alleles A,B,O.

The map file

```
> system("cat blood-data/blood_m6_map.dat")
nloci=6
comment="#"
field_separator=":"
# fictitious blood group data
read=6
0:m0:A:0
1:m1:A:10
2:m2:A:15
3:m3:A:20
4:m4:A:25
5:m5:A:30
```


The marker data file

```
> system("cat blood-data/blood_n4m6.dat")
ploidy=2
nloci=6
nparents=2
nprogeny=4
null_allele="0"
na_phenotype="*"
na_allele="*"
dominant_allele=NULL
allele_separator=","
comment="#"
# blood fictitious marker data
# 6 individuals (2 parents+4progeny)
read=6
# locus 0 @0cM
m0;A;A,B;A;B;A;B
m1;A;A;0;A;A;0
m2;A;B;0;A;B;A,B
m3;*;*;0;A;B;A,B
m4;A;B;0;A;B;A
m5;*;*;0;A;B;A
```


Peeling run (stand-alone program)

See file `blood_n4m6.out`.

```
Usage: peeling map-file marker-file > output-file

> cd visg-course2012/blood-data
> ../software/bin/peeling blood_m6_map.dat  blood_n4m6.dat \
       > blood_n4m6.out
```


Peeling, R/polyploids package

```
> library(polyploids) # may be included in BayesQTLBIC
> # read map file
> blood.map <- polyploids.read.map.file("blood-data/blood_m6_map.dat")
> blood.map
  index marker chrom pos.cM
1     0     m0     A      0
2     1     m1     A     10
3     2     m2     A     15
4     3     m3     A     20
5     4     m4     A     25
6     5     m5     A     30
```

Peeling, R/polyploids package

```
> # read marker file
> blood.markers <- polyploids.read.marker.file("blood-data/blood_n4m6.dat")
> # do peeling
> blood.pl <- polyploids.peeling(blood.map, blood.markers, nsamples=10,
+     min.prob=5e-4, seed=12345, verbose=1)
> # align samples
> blood.pl <- align.peeling(blood.pl)
```


Blood example, single marker peeling

```
allopolyploids peeling: (C) R.D. Ball, Scion/VISG 2011, 2012
 6 loci, 2 parental phenotypes, 4 progeny, ploidy = 2, seed = 12345
 6 loci single marker peeling, 6 loci HMM peeling
*** single marker  peeling for loci:0,1,2,3,4,5
  0: 1 3
  1: 2 3
  2: 1 4
  3: 2 4

single marker peeling:
 *** single marker peeling for locus[0] m0 ***


*
 *** summary data for locus after single marker peeling ***
*

alleles:
0: A
1: B
2: O
parental phenotypes:
```



```
1: A
2: A,B
number of progeny = 4
lc1p->n_unique_phenotypes = 4
table of progeny phenotypes
 i:               yp,    count
 0:                A,        2
 1:              A,B,        0
 2:                B,        2
 3:                O,        0
lc1p->n_genotypes = 9
marginal probabilities for parental genotypes
  i:               mg,              yp,     p1,     p2
  0:              A,A,               A, 0.0000, 0.0000
  1:              A,B,             A,B, 0.0000, 0.5000
  2:              A,O,               A, 0.5000, 0.0000
  3:              B,A,             A,B, 0.0000, 0.5000
. . .
  4:              B,B,               B, 0.0000, 0.0000
  5:              B,O,               B, 0.0000, 0.0000
. . .
  6:              O,A,               A, 0.5000, 0.0000
  7:              O,B,               B, 0.0000, 0.0000
  8:              O,O,               O, 0.0000, 0.0000
marginal probabilities for parental genotype pairs
```



```
(  2,  1):               A,O,             A,B,             A,  0.25000000
(  2,  3):               A,O,             B,A,             A,  0.25000000
(  6,  1):               O,A,             A,B,             A,  0.25000000
(  6,  3):               O,A,             B,A,             A,  0.25000000
locus probs (logfmp1mp2)
:n_genotypes=9, max_log = 0.000000, min_log = -18.420681
(2,1):  -8.553
(2,3):  -8.553
(6,1):  -8.553
(6,3):  -8.553
 *** single marker peeling for locus[1] m1 ***
.
.
.
```

Peeling strategy

Brute force peeling can handle ~ 5 markers in diploids.

Our strategy:

1. single marker peeling
2. identify errors
3. HMM peeling (2 loci to start with)

4. compute probabilities for parental combinations, store non-negligible combinations
5. adding one marker at a time, repeat steps 3,4 for stored parental combinations combined with possibilities for the new marker

Single marker peeling

Peel individual markers separately:

1. For $t = 1, \ldots, T$
   2. Peel marker t
   3. Fix genotype errors, repeat step 2 if necessary
   4. Eliminate low probability parental combinations
   5. Store $\texttt{parental\_combinations}(t)$ and probabilities

↓

HMM peeling

Iterative strategy, $O(N^2T^2)$ per progeny:

1. Let $t \leftarrow 2, \texttt{min\_prob} > 0$, e.g. $\texttt{min\_prob} = 5 \times 10^{-4}$.
2. For $p \in \texttt{parental\_combinations}(1, \ldots, t-1) \times \texttt{parental\_combinations}(t)$
   3. do HMM for loci $1 \ldots t$ for each progeny conditional on p
   4. calculate $\Pr(p) =$ marginal probability from HMM
   5. eliminate low probability combinations ($\Pr(p) < \texttt{min\_prob}$).
6. Store $\texttt{parental\_combinations}(1, \ldots, t)$ and probabilities
7. Increment t and repeat steps 2–6 until $t = T$
8. Sample parental combinations
9. Repeat HMM to sample progeny virtual marker genotypes (g_{ci} in Fig. 1)
10. Align marker phases on samples, group into alignment classes $\mathcal{C}$.

Clover data

White clover (*Trifolium repens*).

Allo-tetraploid: 1234 $\times$ 5678.

- Allo-tetraploid
- $n = 182$ progeny
- Chromosomes A1A2 . . . H1H2

- Up to about 26 markers per chromosome
- diploidised data from Brent
- psuedo-SSR marker calls generated to represent likely raw polyploid data
- traits measured at Lincoln
- seed yield, years 2002–2004 (plus others)

Peeling run (stand-alone program)

```
Usage: peeling map-file marker-file > output-file

e.g.

> ./peeling clover_A1A2_m25_map.dat clover_A1A2n182m25.dat \
        > A1A2_peeling.out
```


Clover C1C2 peeling (within R)

```
> library(polyploids)
> # read map file
> chromC.map.df <- polyploids.read.map.file(map.file=
+      "clover-data/clover_C1C2_m17_map_v2.dat")
> # read marker file
> chromC.marker.data <- polyploids.read.marker.file(marker.file=
+      "clover-data/clover_C1C2n182m17_v2.dat")
> # do peeling
> date()
> # 0:30
> set.seed(12345)
> chromC.peeling <- polyploids.peeling(chromC.map.df,
+      chromC.marker.data, nsamples=10,min.prob=5.0e-4,
+      seed=12345, verbose=1)
> date()
> save(chromC.peeling, file="clover-data/clover_chromC.peeling_v2b.rda")
```


Clover C1C2 alignment

Note: 1 alignment class.

```
> pl1C <- align.peeling(chromC.peeling)
 chr [1:3128] "0,672" "678,676" "0,672,676" "678,676" "-999" ..
.
.
.
> table(pl1C$alignment$alignment.class)

 1
10
```

Single marker peeling for chromosome A1A2

Table 1. Single marker peeling for chromosome A1A2.

locus	phenotype	genotype†	p1 prob. × nreps‡	p2 prob. × nreps‡
0. prs753z				
	753,755	0,0,753,755	0.1462×4	0.1462×4
	753,755	0,753,0,755	0.0497×8	0.0497×8
	753,755	0,753,753,755	0.0022×8	0.0022×8
1. prs089bx				
	95	0,0,0,95	0.25×4	—
	91,97	0,91,0,97	—	0.125×8
2. prs685x				
	685	0,0,0,685	—	0.25×4
	687	0,0,0,687	0.25×4	—
3. ats032x1x2				
	32,40,42	0,32,40,42	0.125×8	—
	36,44	0,36,0,44	—	0.125×8
4. prs10aex				
	20	0,0,0,20	0.25×4	—
	10,18,22	0,10,18,22	—	0.125×8
5. prs112x				
	112,114	0,0,112,114	0.25×4	—
	116,118	0,0,116,118	—	0.25×4
6. prs396d				
	0	0,0,0,0	—	1.0×1
	402	0,0,0,402	0.25×4	—
9. prs504b				
	0	0,0,0,0	1.0×1	—
	506	0,0,0,506	—	0.25×4
10. prs497db				
	0	0,0,0,0	—	1.0×1
	499,503	0,499,0,503	0.125×8	—
23. prs200x1x2				
	200,202,212,214	200,212,202,214	0.125×8	—
	204,206,208,210	204,210,206,208	—	0.125×8
24. prs380xc				
	380,390	0,0,380,390	0.25×4	—
	382,384,388	0,382,384,388,	—	0.1250×8

†Ordered genotypes, only one representative per alignment class per genotype shown.

‡ Number of replicate genotypes equivalent up to alignment permutation, sharing the same probability.

Clover C1C2 parental combinations

Look at parental combinations from peeling (sample 1).

```
> C1C2.Xc <- polyploids.calc.Xc(pl1C)
> postpeeling4(pl1C, C1C2.Xc, plot=TRUE)
     [,1]  [,2]  [,3]  [,4]  [,5]  [,6]  [,7]  [,8]
[1,] "0"   "0"   "0"   "672" "678" "0"   "676" "0"
[2,] "619" "617" "625" "0"   "627" "0"   "621" "629"
[3,] "540" "538" "0"   "0"   "538" "540" "0"   "0"
[4,] "0"   "0"   "0"   "0"   "269" "0"   "0"   "0"
[5,] "639" "645" "0"   "643" "0"   "0"   "0"   "0"
[6,] "616" "618" "0"   "0"   "614" "620" "0"   "0"
[7,] "0"   "0"   "369" "367" "0"   "0"   "367" "369"
```

```
 [8,] "0"   "0"   "0"   "16"  "0"   "0"   "0"   "18"
 [9,] "0"   "0"   "396" "0"   "0"   "0"   "398" "0"
[10,] "0"   "490" "0"   "0"   "0"   "0"   "0"   "0"
[11,] "0"   "0"   "545" "543" "0"   "0"   "0"   "547"
[12,] "0"   "0"   "0"   "0"   "711" "0"   "0"   "0"
[13,] "109" "107" "0"   "0"   "0"   "0"   "0"   "0"
[14,] "516" "0"   "0"   "0"   "0"   "0"   "0"   "0"
[15,] "0"   "296" "0"   "0"   "0"   "298" "0"   "0"
[16,] "736" "0"   "0"   "0"   "0"   "730" "0"   "0"
[17,] "0"   "737" "0"   "0"   "0"   "739" "0"   "745"
```


Clover C1C2 progeny gci's

Cross is 1234 x 5678.

Allo-tetraploids progeny inherit 1 or 2 and 3 or 4 and 5 or 6 and 7 or 8, e.g. 1537, 2548, 2647, 1458.

1 vs 2 is parent 1 subgenome 1
3 vs 4 is parent 1 subgenome 2
5 vs 6 is parent 2 subgenome 1
7 vs 7 is parent 2 subgenome 2

Clover C1C2 progeny gci's

Look at 1st 6 markers as 4 column array:

```
> # a look at peeling output (gci's)
> # ploidy 4 x 182 progeny x 17 markers x 10 samples
> dim(pl1C$progeny.gci)
[1]   4 182  17  10
> # 1st 6 markers, progeny 1
> # 4->3 => recombination between m1 and m2 on parent 1, C2
> # 6->5 => recombination between m3 and m4 on parent 2, C1
> matrix(aperm(pl1C$progeny.gci,c(1,3,2,4)), ncol=4,byrow=TRUE)[1:6,]
     [,1] [,2] [,3] [,4]
[1,]    1    6    4    7
[2,]    1    6    3    7
[3,]    1    6    3    7
[4,]    1    5    3    7
[5,]    1    5    3    7
[6,]    1    5    3    7
```



```
> # 1st 6 markers, progeny 2
> # no recombinations
> matrix(aperm(pl1C$progeny.gci,c(1,3,2,4)), ncol=4,byrow=TRUE)[17+1:6,]
     [,1] [,2] [,3] [,4]
[1,]    1    5    3    7
[2,]    1    5    3    7
[3,]    1    5    3    7
[4,]    1    5    3    7
[5,]    1    5    3    7
[6,]    1    5    3    7
> # 1st 6 markers, progeny 3
> # 5->6 => recombination between m3 and m4 on parent 2, C1
> matrix(aperm(pl1C$progeny.gci,c(1,3,2,4)), ncol=4,byrow=TRUE)[2*17+1:6,]
     [,1] [,2] [,3] [,4]
[1,]    1    5    4    7
[2,]    1    5    4    7
[3,]    1    5    4    7
[4,]    1    6    4    7
[5,]    1    6    4    7
[6,]    1    6    4    7
```

Clover E1E2 alignment

Note: 2 alignment classes.

```
> # Use saved peeling rda file
> attach("clover-data/clover_chromC.peeling_v2.rda")
> ls(pos=2)
[1] "chromE.peeling"
> pl1E <- align.peeling(chromE.peeling)
 chr [1:3128] "37" "0" "37" "37" "0" "37" "37" "-999" ...
Read 184 items
.
.
.
```



```
*** initial phase alignment for sample  2  ***
locus: 1
.unaligned parental genotypes:
     [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8]
[1,] "0"  "0"  "0"  "1"  "0"  "0"  "0"  "0"
[2,] "1"  "0"  "0"  "0"  "0"  "0"  "0"  "0"
.
.
.
permutations aligning loci 1, ... ,  16
     [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8]
[1,]    3    4    2    1    8    7    6    5
locus: 17
.unaligned parental genotypes:
     [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8]
```



```
[1,] "0"  "0"  "1"  "0"  "0"  "0"  "0"  "0"
[2,] "0"  "1"  "0"  "0"  "0"  "0"  "0"  "0"
.
.
.

.unaligned parental genotypes:
     [,1] [,2] [,3] [,4] [,5] [,6] [,7] [,8]
[1,] "0"  "0"  "0"  "1"  "0"  "0"  "0"  "2"
[2,] "0"  "0"  "0"  "1"  "0"  "0"  "2"  "0"
permutations aligning loci 1, ... ,  6
< nil >
sample **  2  ** could not be aligned at locus:  6
samples aligned at loci 1 2 3 4 5
[1] 1 2
```



```
alignment.class
1 2
9 1
.
.
.
> table(pl1E$alignment$alignment.class)

1 2
9 1
```

Part II: QTL analysis with BayesQTLBIC

Theory

Ball Genetics 2001, 2007. R package BayesQTLBIC.

- X matrix of marker contrasts
- multiple models $\leftrightarrow$ selected sets of columns of X
- prior probabilities proportional to marker spacing, expected number of QTL
- approximate probabilities for models from BIC criterion

- consider models $\mathcal{M}_\gamma$ according to posterior probabilities

$$\mathcal{M}_\gamma : \; y \; = X_\gamma b_\gamma + e \tag{9}$$

$$\Pr(\mathcal{M}_\gamma \mid y) \; \approx \exp(-\text{BIC}/2) \times \text{prior} \tag{10}$$

Theory

Interpretation:

- marker m_i selected in $\mathcal{M}_\gamma \leftrightarrow$ QTL in vicinity of m_i.
- $b_{\gamma,i}$ is the causal effect of m_i assuming $\mathcal{M}_\gamma$ is the true model.
- compute model averaged quantities
- Pr(QTL $\in$ region)

- probabilities for number of QTL

BayesQTLBIC R package

Key functions:

- `bicreg.qtl()`: analysis for a set of loci, e.g. 1 chromosome
- `bicreg.models()`: combine analyses from `bicreg.qtl()`, e.g. from separate chromosomes
- `summary()`: summary method

BIC method for polyploids QTL mapping

- R package `BayesQTLBIC` (Ball 2001, 2009).
- Poisson prior, $n_{QTL} \sim \text{Poisson}(\lambda_Q)$, e.g. $\lambda_Q = 10$
- Prior probability per marker is proportional to marker spacing, λ_Q
- Populate model matrix $X^{(s)}$ with contrasts from virtual marker genotypes from peeling samples $s = 1, \ldots, n_s$
- Use multiple imputation for each alignment class $\mathcal{C}$
  - + combine X^s, for $s \in \mathcal{C}$ by row, to form X.
  - + choose search strategy e.g.
    - – exhaustive by chromosome/subgenome/parent, or,
    - – exhaustive by genomic window/subgenome/parent, and/or
    - – limit model size, e.g. ≤ 3 QTL per chromosome
  - + search through space of models $\mathcal{M}_\gamma : y = X_\gamma \beta_\gamma + \epsilon$, $X_\gamma \leftrightarrow$ selected columns of $X \leftrightarrow$ putative QTL
  - + compute: $\Pr(\mathcal{M}_\gamma) \propto \exp(-\text{BIC}/2) \times$ prior, for models
  - + compute summaries of interest e.g.

$$\Pr(\text{QTL in region}) = \sum \{\Pr(\mathcal{M}_\gamma) \text{ with QTL in region}\} \quad (1)$$

  - + sample from models for each chromosome and recalculate probabilities for a 'genome-wide' analysis (optional).
- Combine information across alignment classes

Clover QTL mapping data

```
> clover.traits.n182.df[1:5,c(1,4:6)]
      Entry LR02_SEEDWGT LR03_SEEDWGT LR04_SEEDWGT
1 clover001         7.17         5.93         2.40
2 clover002        11.60         6.07         2.42
3 clover003        16.17        19.63        11.70
4 clover004        15.67        10.67         4.67
5 clover005        23.07        13.70         6.17
> # seed weight traits
> Y <- clover.traits.n182.df[,c("LR02_SEEDWGT",
+           "LR03_SEEDWGT","LR04_SEEDWGT")]
> seedwt <- apply(Y,1,mean)
> seedwt02 <- clover.traits.n182.df[,"LR02_SEEDWGT"]
> seedwt04 <- clover.traits.n182.df[,"LR04_SEEDWGT"]
```

QTL analysis for clover C1C2– Separate analysis by subgenome/parent.

- Key function `bicreg.qtl`.

- Uses `pl1C` from peeling.

```
> library(BayesQTLBIC)
> nloci <- length(pl1C$locus.names)
> nsamples <- 10
> # calculate prior
> C1C2.prior <- polyploids.calc.prior(pos.cM=pl1C$locus.pos.cM,
+      prior.rate=10, genome.length.cM=591)
```



```
> # calculate X-matrix, contrasts from progeny
> # virtual marker genotypes (gci)
> # separate analyses by chromosome/parent/subgenome
> # i.e. virtual marker genotypes
> C1C2.Xc <- polyploids.calc.Xc(pl1C)
> # 1 vs. 2 (p1, C1)
> C1C2.seedwt02.res1 <- bicreg.qtl(C1C2.Xc[,1:nloci],
+     y=rep(seedwt02,nsamples), num.imputations=nsamples,
+     prior=C1C2.prior)
> # 5 vs. 6 (p2, C1)
> C1C2.seedwt02.res2 <- bicreg.qtl(C1C2.Xc[,nloci+1:nloci],
+     y=rep(seedwt02,nsamples), num.imputations=nsamples,
+     prior=C1C2.prior)
```



```
> # 3 vs. 4 (p1, C2)
> C1C2.seedwt02.res3 <- bicreg.qtl(C1C2.Xc[,2*nloci+1:nloci],
+     y=rep(seedwt02,nsamples), num.imputations=nsamples,
+     prior=C1C2.prior)
> # 7 vs. 8 (p2, C2)
> C1C2.seedwt02.res4 <- bicreg.qtl(C1C2.Xc[,3*nloci+1:nloci],
+     y=rep(seedwt02,nsamples), num.imputations=nsamples,
+     prior=C1C2.prior)
```


QTL analysis for clover C1C2—summary output

- Look at top 10 models with `summary()`

- Note low probability 3.7×10^{-7} for model size 0 $\Rightarrow$ strong evidence for QTL.

```
> summary(C1C2.seedwt02.res4, nbest=10)
R-squared, BIC, and approximate posterior probabilties for individual models
   X4m1 X4m2 X4m3 X4m4 X4m5 X4m6 X4m7 X4m8 X4m9 X4m10 X4m11 X4m12 X4m13 X4m1
1     0    0    0    0    0    0    1    0    0     0     0     0     0
2     0    0    0    0    0    0    1    0    0     0     0     0     0
3     0    0    0    0    0    0    1    0    0     0     0     0     0
4     0    0    0    0    0    0    1    0    0     0     0     0     0
5     0    0    0    0    0    0    1    0    0     0     0     0     0
6     0    0    0    0    0    0    1    0    0     0     0     0     1
7     0    0    0    0    0    0    1    0    0     0     1     0     0
```

```
8     0    0    0    0    0    0    1    0    0     1     0     0     0
9     0    0    0    0    0    0    1    1    0     0     0     0     0
10    0    0    0    0    0    0    1    0    0     0     0     1     0
   X4m15 X4m16 X4m17     R2       BIC   postprob   cumprob
1      0     0     0 18.961 -25.34475 0.50292851 0.5029285
2      0     1     0 22.905 -23.47481 0.19744843 0.7003769
3      0     0     1 22.946 -21.60274 0.07743553 0.7778125
4      1     0     0 21.573 -21.07197 0.05938596 0.8371984
5      0     0     0 21.299 -20.78715 0.05150353 0.8887020
6      0     0     0 20.874 -19.62150 0.02875532 0.9174573
7      0     0     0 20.748 -18.79274 0.01900009 0.9364574
8      0     0     0 20.661 -18.60854 0.01732837 0.9537858
9      0     0     0 19.760 -17.96640 0.01256954 0.9663553
10     0     0     0 20.636 -17.77004 0.01139409 0.9777494
```



```
marginal probabilities for model sizes
          0           1           2           3           4
3.720903e-07 5.031256e-01 4.846549e-01 1.212378e-02 9.534188e-05
marginal probabilities for individual variables
      X4m7      X4m14      X4m15      X4m16      X4m17
0.97774939 0.05150353 0.05938596 0.19744843 0.07743553
attr,"prior")
 [1] 0.07380106 0.11930084 0.14852022 0.12570141 0.07888157 0.07290340
 [7] 0.08218792 0.12038065 0.06696074 0.06324747 0.06279026 0.04369076
[13] 0.08065201 0.08780076 0.07476120 0.05349705 0.02068211
attr,"intercept")
[1] TRUE
```


QTL analysis for clover C1C2—Bayes factors by chromosome

$$B = \frac{\Pr(H_1 \mid y)}{\Pr(H_0 \mid y)} \times \frac{\pi(H_0)}{\pi(H_1)} \qquad (11)$$

```
> calc.bf.chrom(pH0=C1C2.seedwt02.res1$postprob.size["0"], prior=C1C2.prior)
        0
0.4071328
> calc.bf.chrom(pH0=C1C2.seedwt02.res2$postprob.size["0"], prior=C1C2.prior)
         0
0.04090569
> calc.bf.chrom(pH0=C1C2.seedwt02.res3$postprob.size["0"], prior=C1C2.prior)
         0
0.02443742
> calc.bf.chrom(pH0=C1C2.seedwt02.res4$postprob.size["0"], prior=C1C2.prior)
       0
829605.7
```


Combined analysis with `bicreg.models()`

- Sample models from each fit.
- Combine samples across fits.
- Re-evaluate probabilities

```
> # combined analysis using bicreg.models()
> C1C2.seedwt02.fits <- list(C1C2.seedwt02.res1,C1C2.seedwt02.res2,
+       C1C2.seedwt02.res3,C1C2.seedwt02.res4)
> nsim <- 1000
> mWhich <- sample.bicreg.qtl.models(C1C2.seedwt02.fits,nsim=nsim)
> date() # 4 mins.
> C1C2.seedwt02.mbic <- bicreg.models(x=C1C2.Xc,y=rep(seedwt02,nsamples),
+       which=mWhich,prior=C1C2.prior,num.imputations=nsamples)
> date()
```

```
> attach("./clover-data/C1C2.seedwt02.mbic.rda")
> summary(C1C2.seedwt02.mbic,nbest=20,min.marker.prob=0.05)
R-squared, BIC, and approximate posterior probabilties for individual models
   1m1 1m2 1m3 1m4 1m5 1m6 1m7 1m8 1m9 1m10 1m11 1m12 1m13 1m14 1m15 1m16 1m
1    0   0   0   0   1   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   1   0   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   0   0   0    0    0    0    0    1    0    0
4    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
.
.
.
   2m1 2m2 2m3 2m4 2m5 2m6 2m7 2m8 2m9 2m10 2m11 2m12 2m13 2m14 2m15 2m16 2m
1    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
4    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
.
.
.


   3m1 3m2 3m3 3m4 3m5 3m6 3m7 3m8 3m9 3m10 3m11 3m12 3m13 3m14 3m15 3m16 3m
```



```
1    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
4    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
.
.
.
   4m1 4m2 4m3 4m4 4m5 4m6 4m7 4m8 4m9 4m10 4m11 4m12 4m13 4m14 4m15 4m16 4m
1    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    1
2    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    0
4    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    0
.
.
.
     R2       BIC    postprob    cumprob
1  28.24 -17.74027 0.072279168 0.07227917
2  23.64 -17.38259 0.060442644 0.13272181
3  23.51 -17.30671 0.058192434 0.19091425
4  18.96 -16.67581 0.042449194 0.23336344
5  27.79 -16.43196 0.037576699 0.27094014
```



```
6  23.11 -16.17196 0.032995904 0.30393604
7  23.44 -16.07551 0.031442334 0.33537838
8  23.12 -15.97683 0.029928696 0.36530707
9  28.28 -15.87287 0.028412673 0.39371975
10 27.48 -15.87111 0.028387695 0.42210744
11 27.39 -15.83084 0.027821917 0.44992936
12 22.90 -14.79631 0.016585995 0.46651535
13 27.39 -14.76612 0.016337527 0.48285288
14 26.70 -14.59058 0.014964671 0.49781755
15 27.82 -14.53871 0.014581578 0.51239913
16 22.41 -14.35808 0.013322358 0.52572149
17 23.41 -14.03532 0.011336917 0.53705840
18 27.44 -13.98734 0.011068130 0.54812653
19 27.50 -13.95243 0.010876628 0.55900316
20 26.22 -13.75258 0.009842327 0.56884549
marginal probabilities for model sizes
           0           1           2           3           4
3.144121e-08 4.244919e-02 3.102480e-01 5.287792e-01 1.178055e-01 7.178861e-0
           6
2.409075e-07
marginal probabilities for individual variables
```



```
      1m5         1m6         1m13        1m14        4m7         4m16        4m17
0.18594148 0.08208697 0.07226023 0.09708248 0.56884549 0.19898900 0.06493901
attr,"prior")
 [1] 0.07380106 0.11930084 0.14852022 0.12570141 0.07888157 0.07290340
 [7] 0.08218792 0.12038065 0.06696074 0.06324747 0.06279026 0.04369076
[13] 0.08065201 0.08780076 0.07476120 0.05349705 0.02068211
attr,"intercept")
[1] TRUE
```

Combined analysis with `bicreg.pppeeling()`

```
> cloverC.seedwt02.bic <- bicreg.pppeeling(y=seedwt02, pl1C,
+       prior.rate=20, genome.length.cM=591, nsim=100)
> summary(cloverC.seedwt02.bic, nbest=38)
R-squared, BIC, and approximate posterior probabilties for individual models
   1m1 1m2 1m3 1m4 1m5 1m6 1m7 1m8 1m9 1m10 1m11 1m12 1m13 1m14 1m15 1m16 1m
1    0   0   0   0   1   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   0   1   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   1   0   0   0   0    0    0    0    0    0    0    0
.
.
.
   2m1 2m2 2m3 2m4 2m5 2m6 2m7 2m8 2m9 2m10 2m11 2m12 2m13 2m14 2m15 2m16 2m
1    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
.
.
.
   3m1 3m2 3m3 3m4 3m5 3m6 3m7 3m8 3m9 3m10 3m11 3m12 3m13 3m14 3m15 3m16 3m
```



```
1    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
2    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
3    0   0   0   0   0   0   0   0   0    0    0    0    0    0    0    0
   4m1 4m2 4m3 4m4 4m5 4m6 4m7 4m8 4m9 4m10 4m11 4m12 4m13 4m14 4m15 4m16 4m
1    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    1
2    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    1
3    0   0   0   0   0   0   1   0   0    0    0    0    0    0    0    0
.
.
.
      R2        BIC    postprob   cumprob
1  28.24 -10.570756 0.153251940 0.1532519
2  27.79  -9.255728 0.079405630 0.2326576
3  23.64  -8.771042 0.062316521 0.2949741
4  23.51  -8.705317 0.060301906 0.3552760
5  27.39  -8.671485 0.059290438 0.4145664
6  27.39  -7.568496 0.034156517 0.4487230
7  23.11  -7.562423 0.034052963 0.4827759
8  26.70  -7.444544 0.032103893 0.5148798
9  30.71  -7.437330 0.031988307 0.5468681
10 23.44  -7.435846 0.031964576 0.5788327
```



```
11 23.12  -7.358564 0.030752992 0.6095857
12 27.82  -7.327749 0.030282796 0.6398685
13 27.44  -6.793248 0.023180917 0.6630494
14 27.50  -6.750191 0.022687206 0.6857366
15 30.06  -6.647346 0.021550053 0.7072867
16 18.96  -6.594120 0.020984109 0.7282708
17 26.77  -6.371281 0.018771614 0.7470424
18 26.53  -6.163801 0.016921855 0.7639642
19 22.90  -6.156653 0.016861480 0.7808257
20 26.03  -5.838770 0.014383628 0.7952093
21 30.16  -5.821093 0.014257058 0.8094664
22 27.43  -5.665178 0.013187828 0.8226542
23 29.73  -5.590516 0.012704594 0.8353588
24 30.75  -5.538818 0.012380401 0.8477392
25 26.74  -5.510335 0.012205331 0.8599445
26 25.69  -5.124997 0.010066407 0.8700110
27 29.00  -4.950675 0.009226162 0.8792371
28 22.05  -4.527381 0.007466273 0.8867034
29 26.81  -4.467113 0.007244641 0.8939480
30 25.47  -4.415860 0.007061344 0.9010094
31 25.28  -4.367444 0.006892456 0.9079018
```



```
32 22.95  -4.271112 0.006568342 0.9144702
33 26.57  -4.259309 0.006529692 0.9209999
34 25.60  -4.239187 0.006464326 0.9274642
35 22.25  -4.192555 0.006315349 0.9337795
36 28.69  -4.030877 0.005824912 0.9396045
37 21.57  -3.782131 0.005143690 0.9447481
38 25.18  -3.702885 0.004943867 0.9496920
marginal probabilities for model sizes
          0           1           2           3           4
7.438204e-09 2.098411e-02 2.747538e-01 5.816783e-01 1.214279e-01 1.155234e-0
          6
7.114546e-07
marginal probabilities for individual variables
       1m5        1m6       1m13       1m14       1m16        4m7       4m15
0.35847453 0.15964234 0.09267385 0.14966572 0.14439901 0.94969201 0.05163121
      4m16       4m17
0.48641589 0.12206182
attr,"prior")
 [1] 0.14215551 0.22436898 0.27498219 0.23560198 0.15154083 0.14049189
 [7] 0.15762098 0.22626980 0.12943773 0.12249470 0.12163790 0.08547263
[13] 0.15479928 0.16789255 0.14393316 0.10413216 0.04093647 0.14215551
```

```
[19] 0.22436898 0.27498219 0.23560198 0.15154083 0.14049189 0.15762098
[25] 0.22626980 0.12943773 0.12249470 0.12163790 0.08547263 0.15479928
[31] 0.16789255 0.14393316 0.10413216 0.04093647 0.14215551 0.22436898
[37] 0.27498219 0.23560198 0.15154083 0.14049189 0.15762098 0.22626980
[43] 0.12943773 0.12249470 0.12163790 0.08547263 0.15479928 0.16789255
[49] 0.14393316 0.10413216 0.04093647 0.14215551 0.22436898 0.27498219
[55] 0.23560198 0.15154083 0.14049189 0.15762098 0.22626980 0.12943773
[61] 0.12249470 0.12163790 0.08547263 0.15479928 0.16789255 0.14393316
[67] 0.10413216 0.04093647
attr,"intercept")
[1] TRUE
```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