

Mapping multiple QTL in experimental crosses

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[→ Teaching → Miscellaneous lectures]

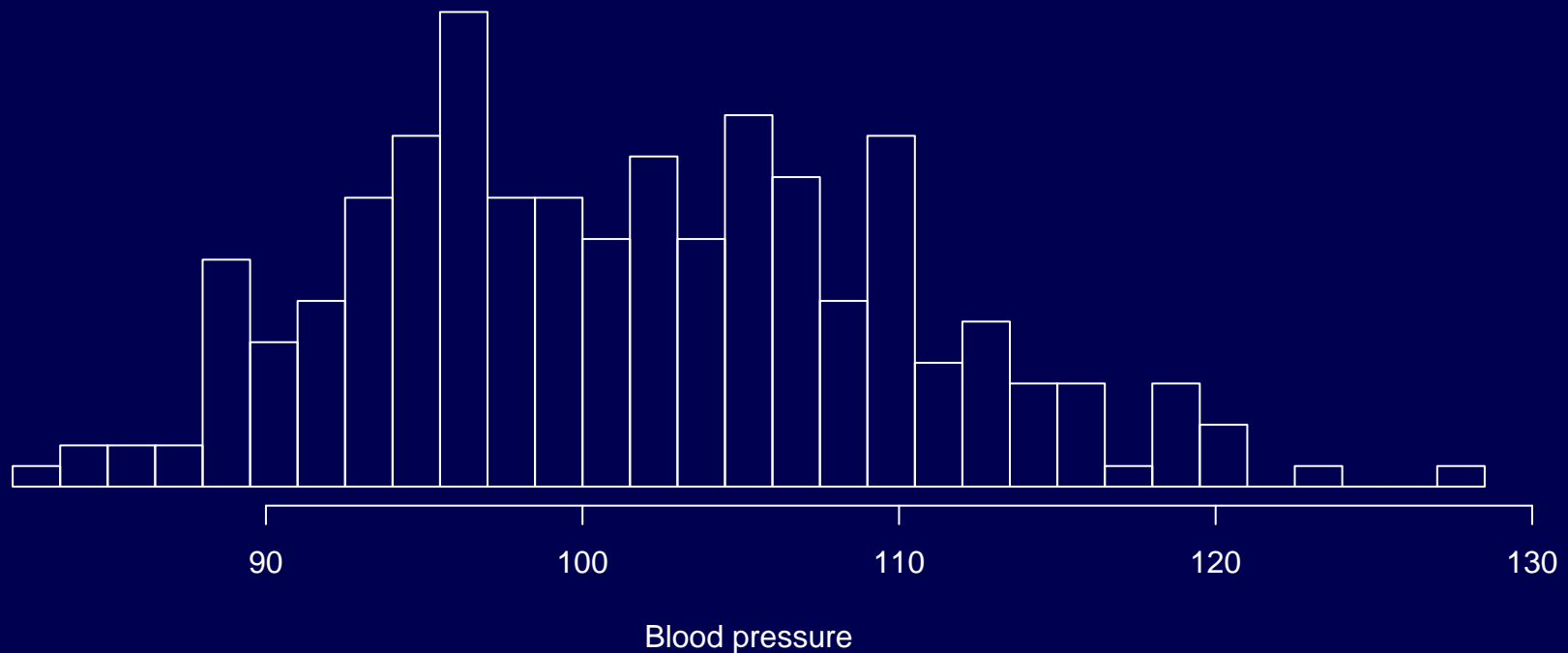


Example

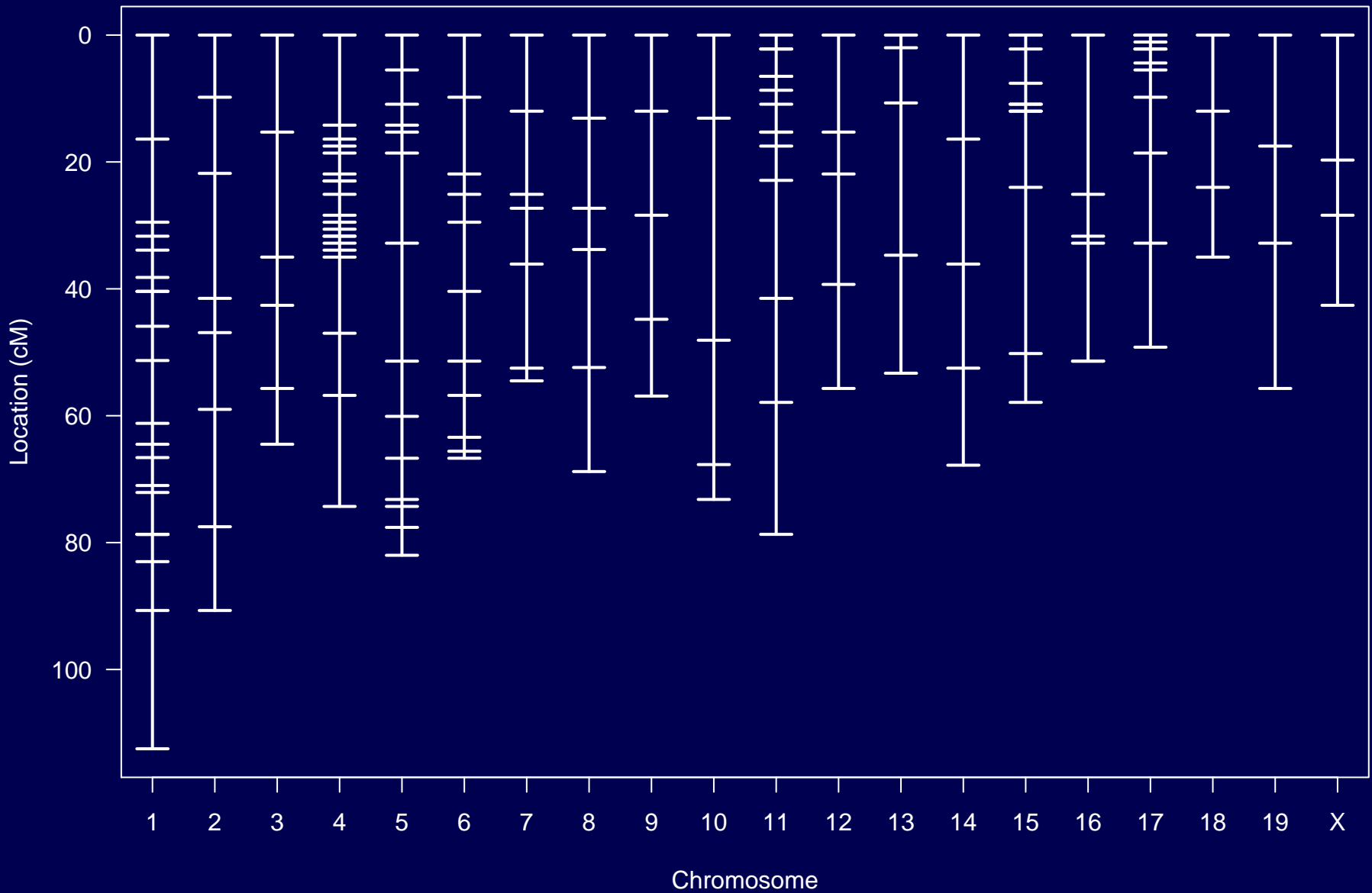
Sugiyama et al. Genomics 71:70-77, 2001

250 male mice from the backcross $(A \times B) \times B$

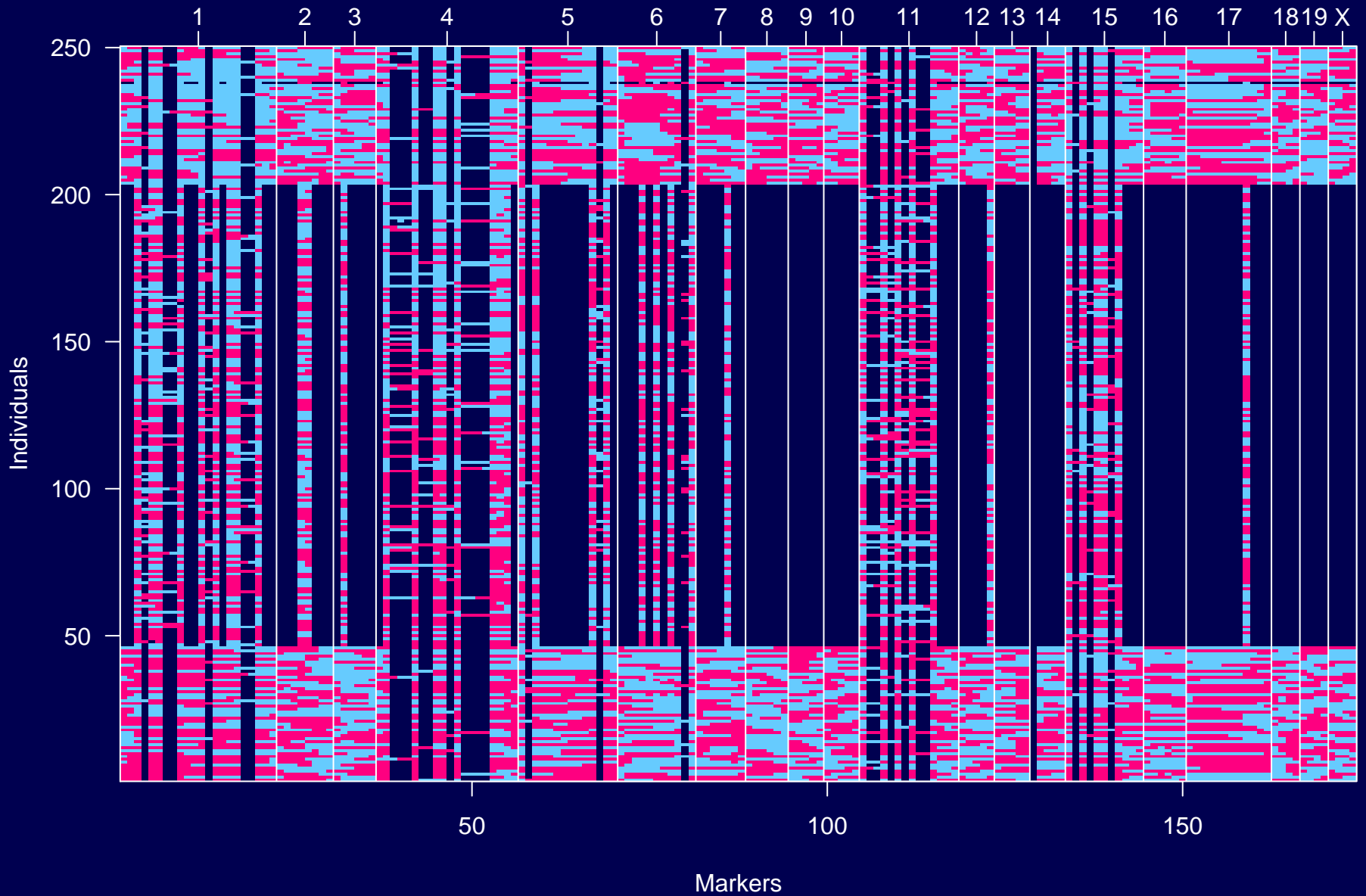
Blood pressure after two weeks drinking water with 1% NaCl



Genetic map



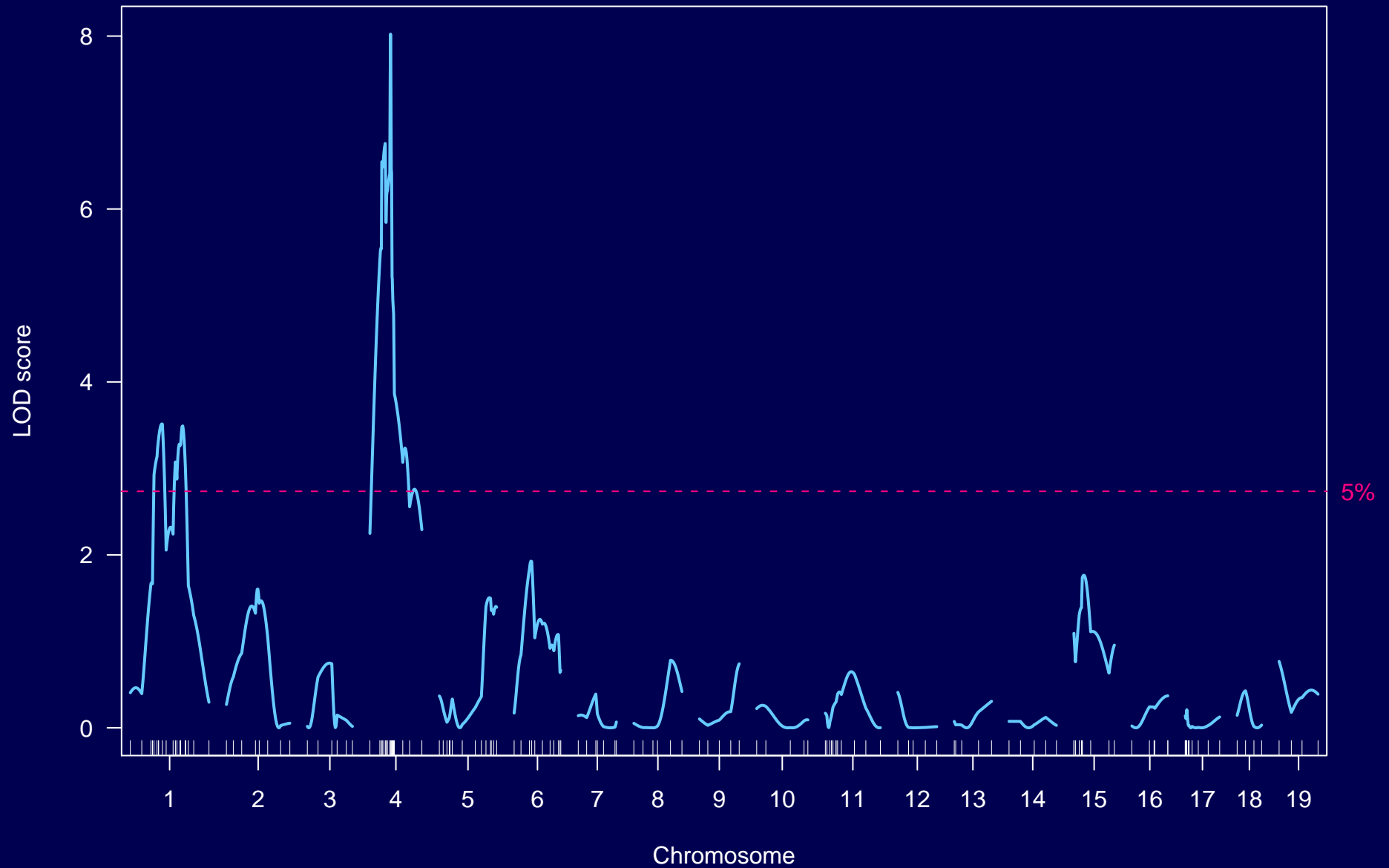
Genotype data



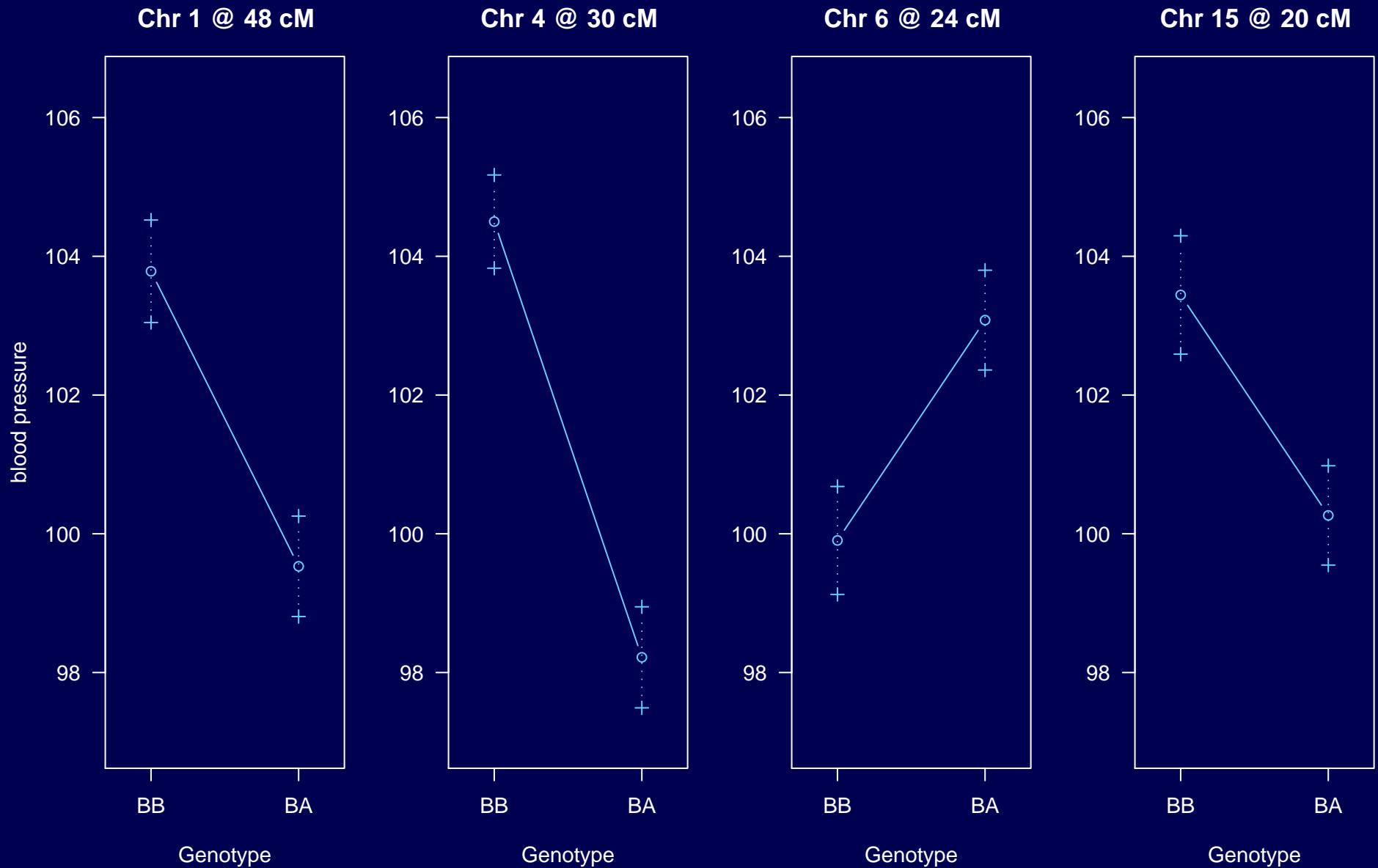
Goals

- Identify quantitative trait loci (QTL)
(and interactions among QTL)
- Interval estimates of QTL location
- Estimated QTL effects

LOD curves



Estimated effects



Modeling multiple QTL

- Reduce residual variation \longrightarrow increased power
- Separate linked QTL
- Identify interactions among QTL (epistasis)

2-dim, 2-QTL scan

For all pairs of positions, fit the following models:

$$H_f : y = \mu + \beta_1 q_1 + \beta_2 q_2 + \gamma q_1 q_2 + \epsilon$$

$$H_a : y = \mu + \beta_1 q_1 + \beta_2 q_2 + \epsilon$$

$$H_1 : y = \mu + \beta_1 q_1 + \epsilon$$

$$H_0 : y = \mu + \epsilon$$

\log_{10} likelihoods:

$$l_f(s, t)$$

$$l_a(s, t)$$

$$l_1(s)$$

$$l_0$$

2-dim, 2-QTL scan

LOD scores:

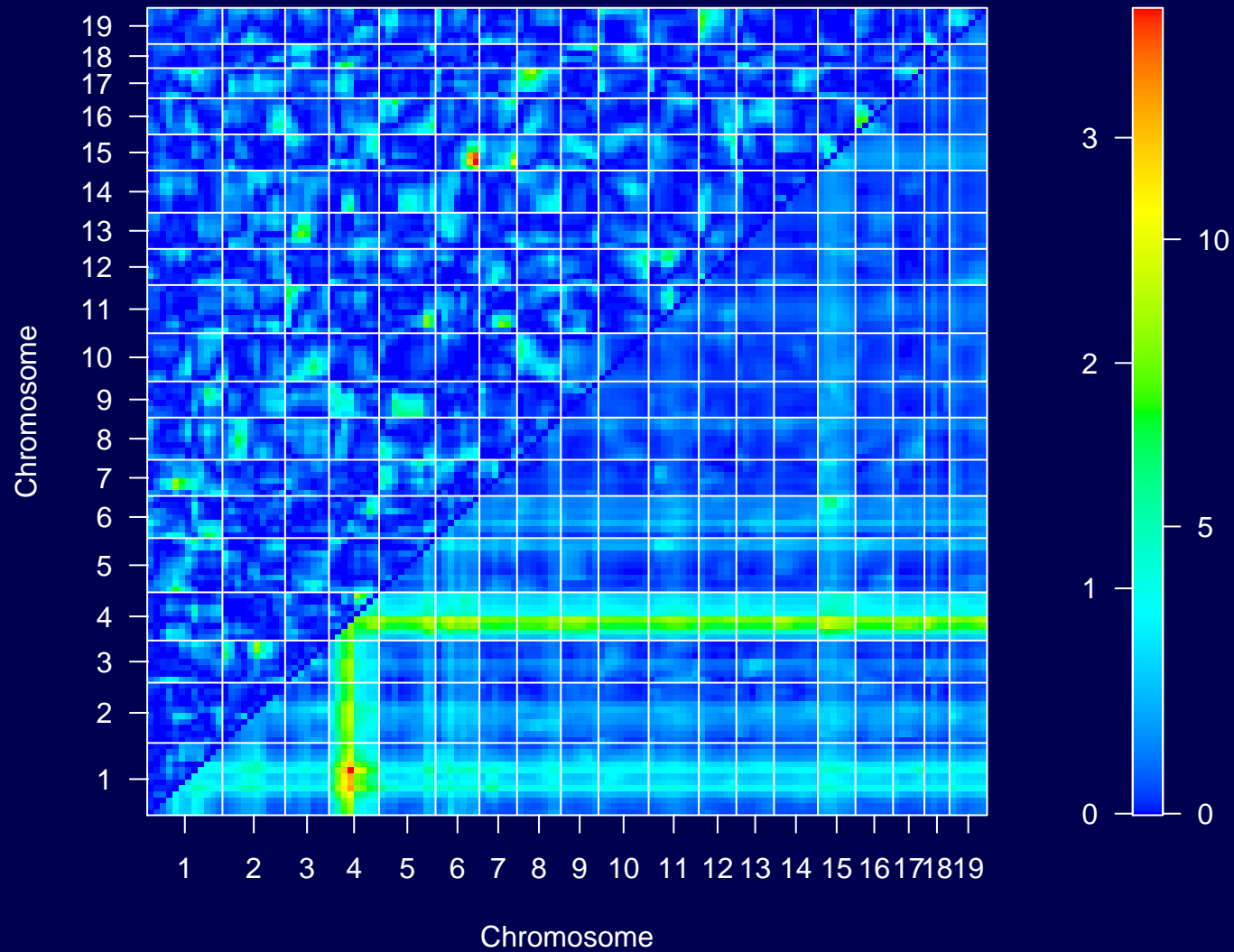
$$\text{LOD}_f(s, t) = l_f(s, t) - l_0$$

$$\text{LOD}_a(s, t) = l_a(s, t) - l_0$$

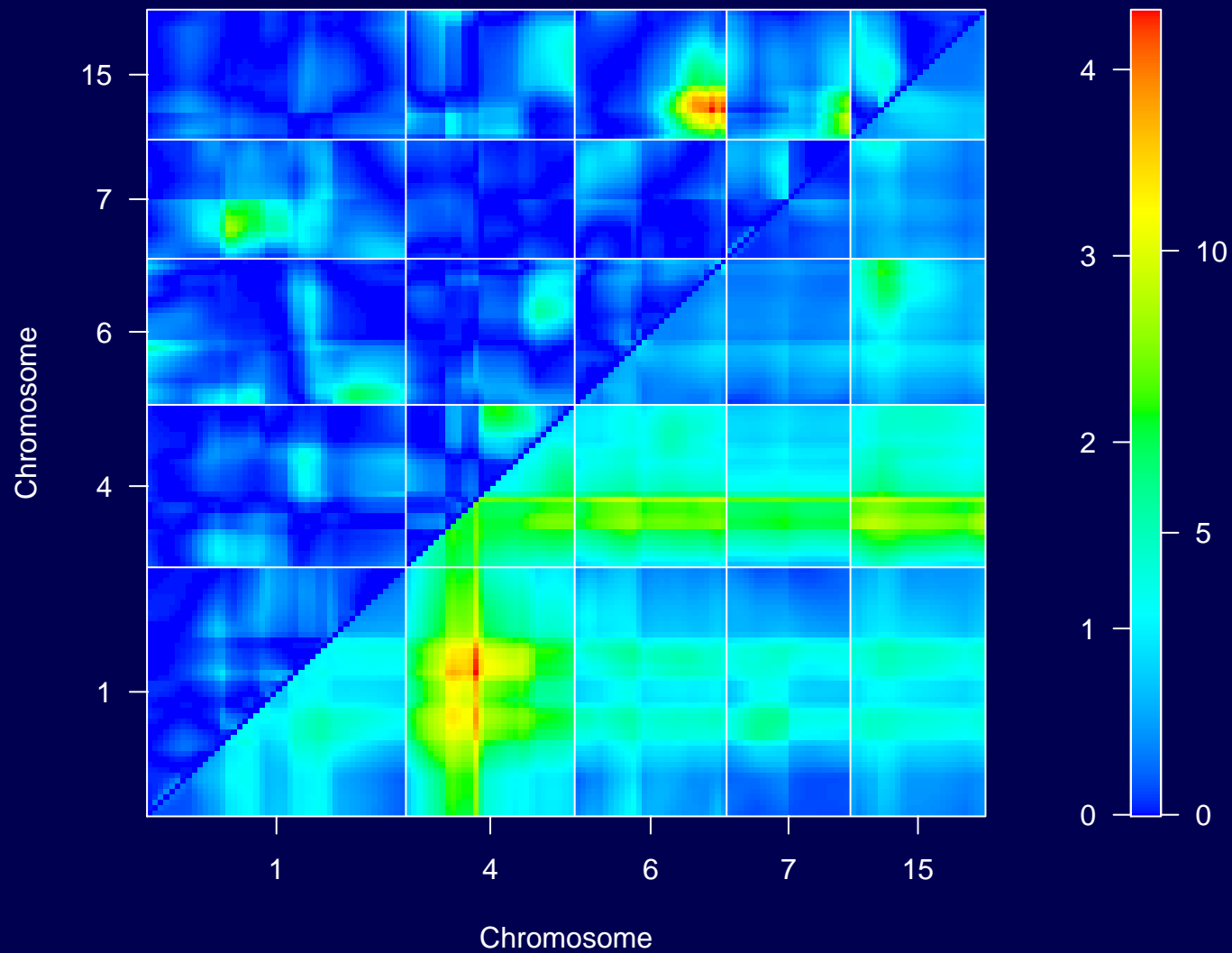
$$\text{LOD}_i(s, t) = l_f(s, t) - l_a(s, t)$$

$$\text{LOD}_1(s) = l_1(s) - l_0$$

Results: LOD_i and LOD_f



Results: LOD_i and LOD_f



Summaries

Consider each pair of chromosomes, (j, k) ,
and let $c(s)$ denote the chromosome for position s .

$$M_f(j, k) = \max_{c(s)=j, c(t)=k} \text{LOD}_f(s, t)$$

$$M_a(j, k) = \max_{c(s)=j, c(t)=k} \text{LOD}_a(s, t)$$

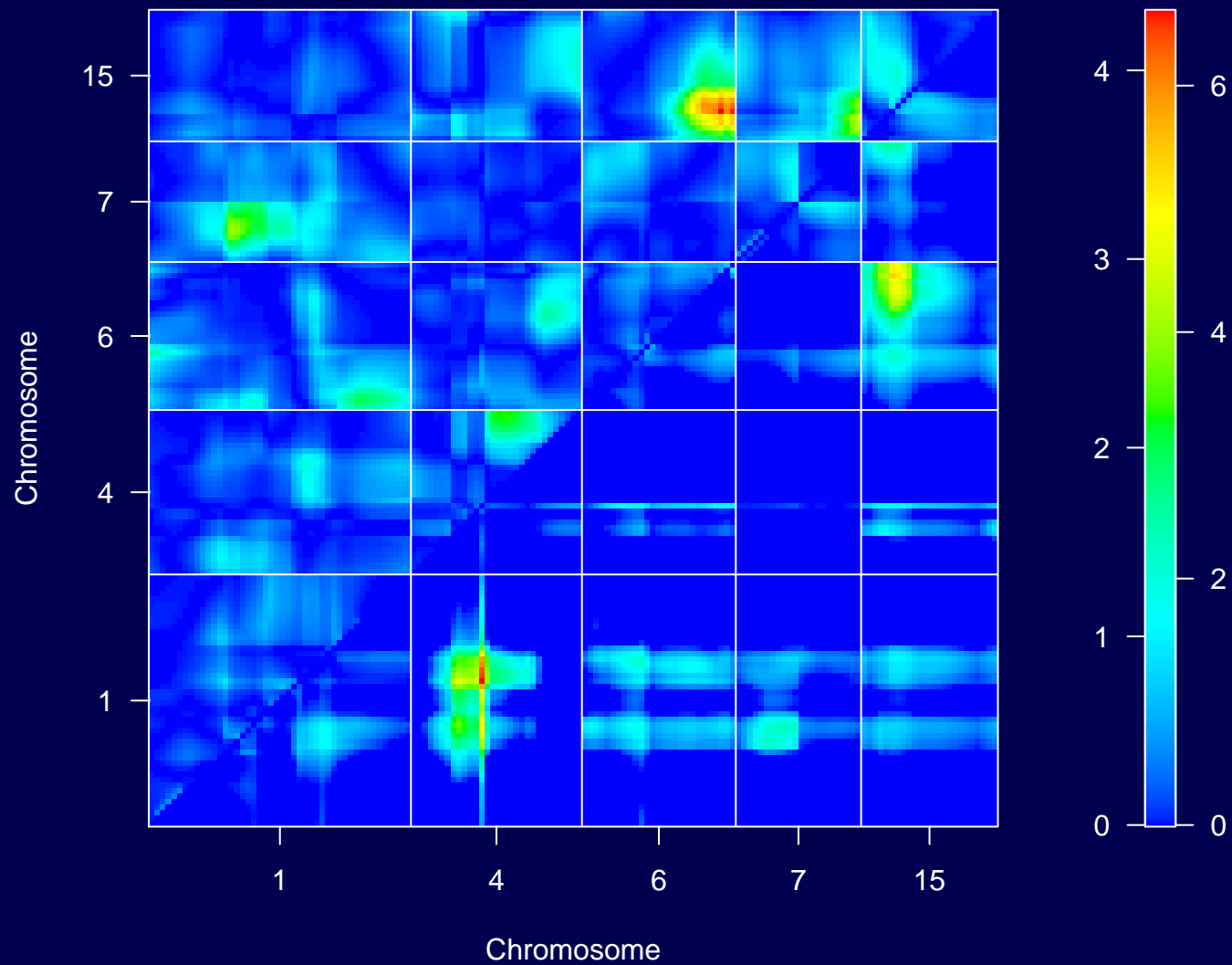
$$M_1(j, k) = \max_{c(s)=j \text{ or } k} \text{LOD}_1(s)$$

$$M_i(j, k) = M_f(j, k) - M_a(j, k)$$

$$M_{fv1}(j, k) = M_f(j, k) - M_1(j, k)$$

$$M_{av1}(j, k) = M_a(j, k) - M_1(j, k)$$

Results: LOD_i and LOD_{fv1}



Thresholds

A pair of chromosomes (j, k) is considered interesting if:

$$M_f(j, k) > T_f \quad \text{and} \quad \{ M_{fv1}(j, k) > T_{fv1} \text{ or } M_i(j, k) > T_i \}$$

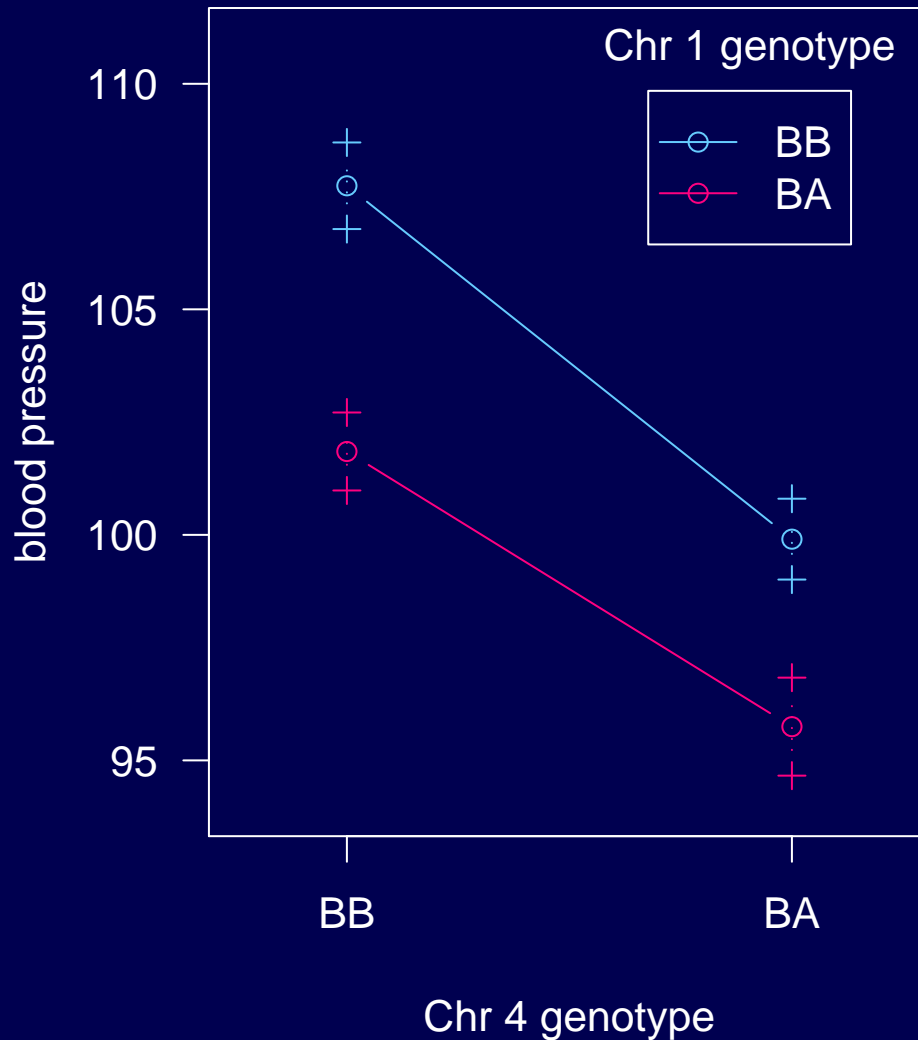
or

$$M_a(j, k) > T_a \quad \text{and} \quad M_{av1}(j, k) > T_{av1}$$

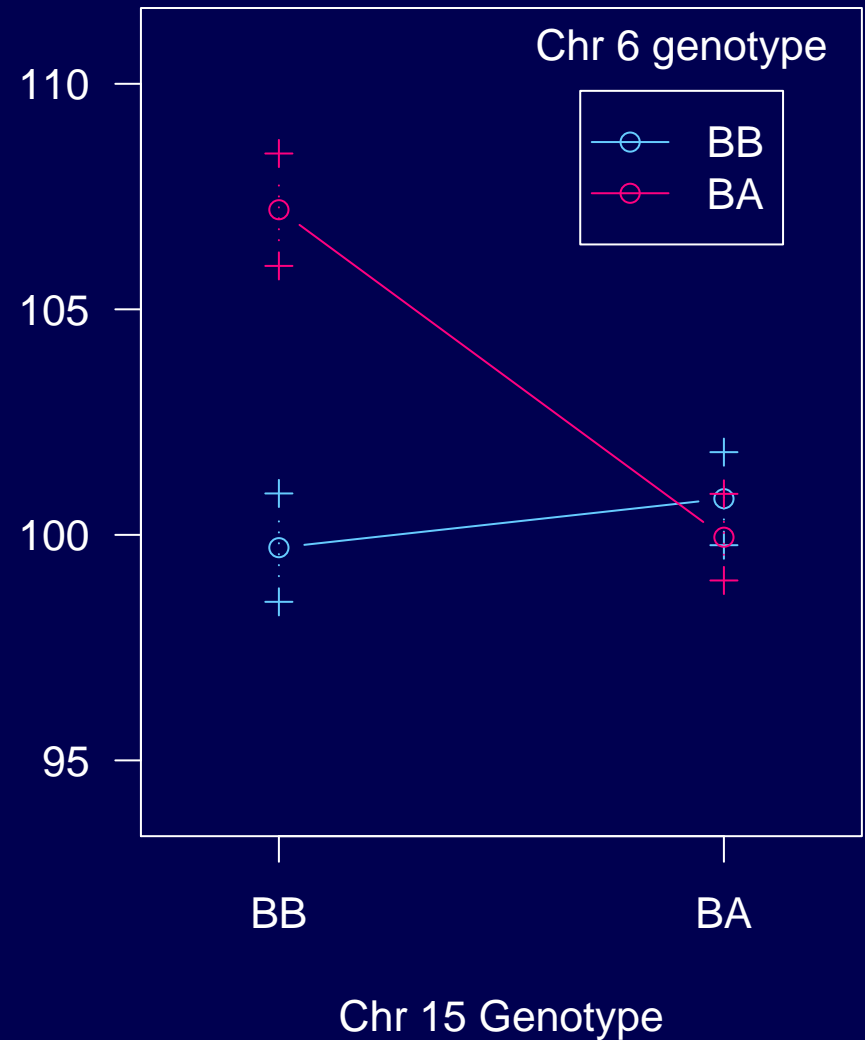
where the thresholds $(T_f, T_{fv1}, T_i, T_a, T_{av1})$ are determined by a permutation test with a 2d scan

Estimated effects

1 x 4



6 x 15



Chr 1: LOD_i and LOD_{av1}

