

QTL mapping in multi-parent populations

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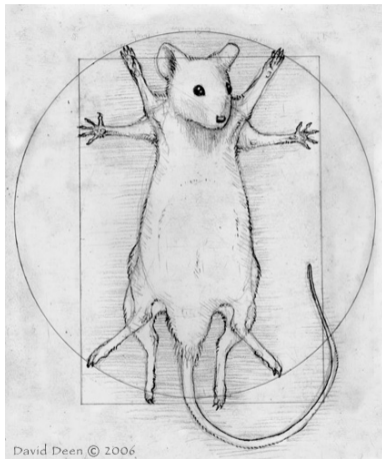
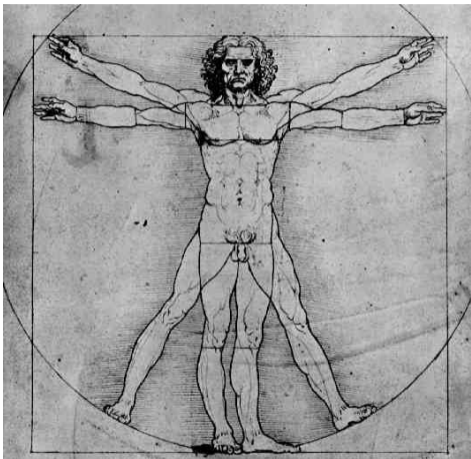
`github.com/kbroman`

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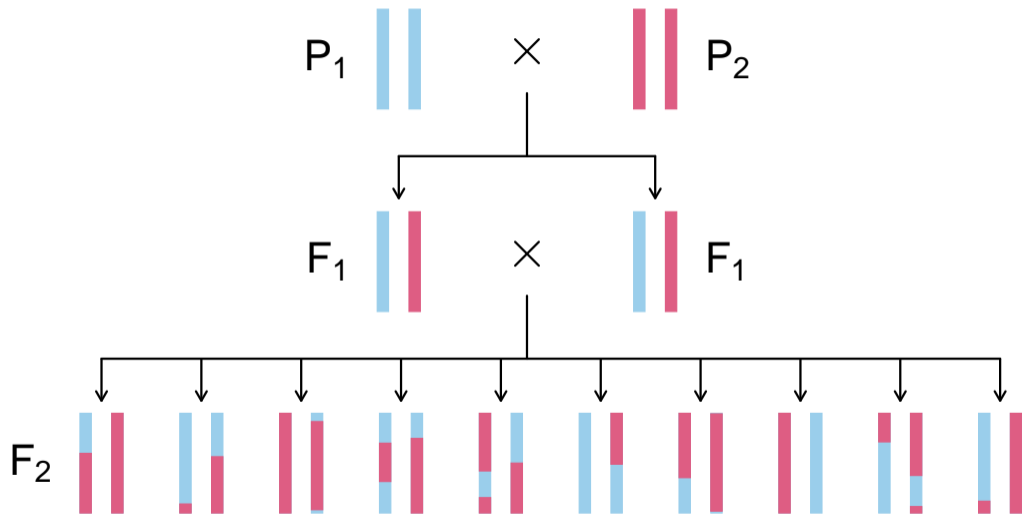




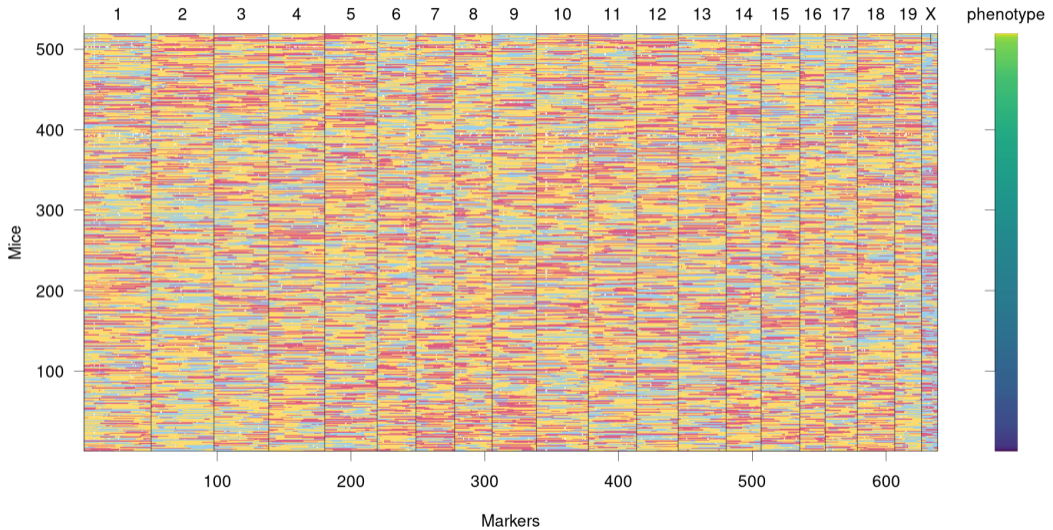


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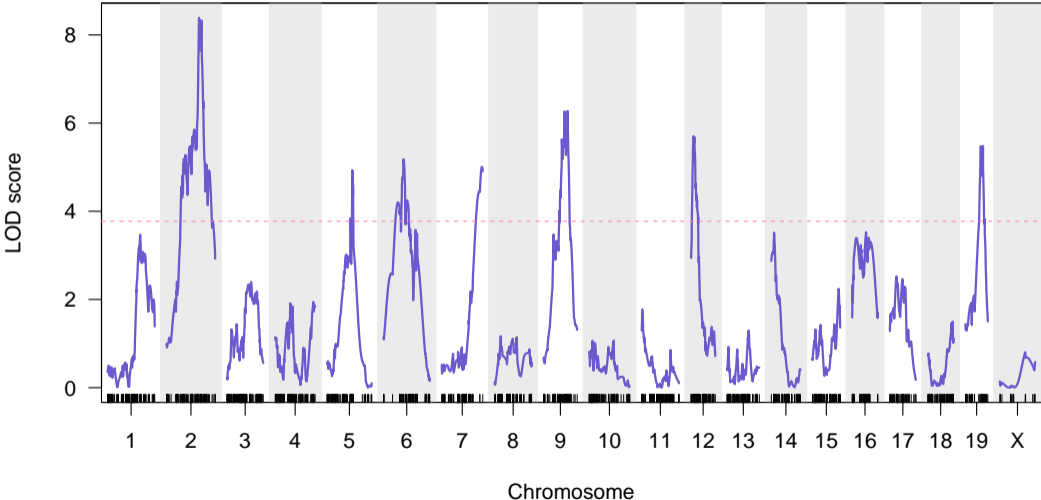
Intercross



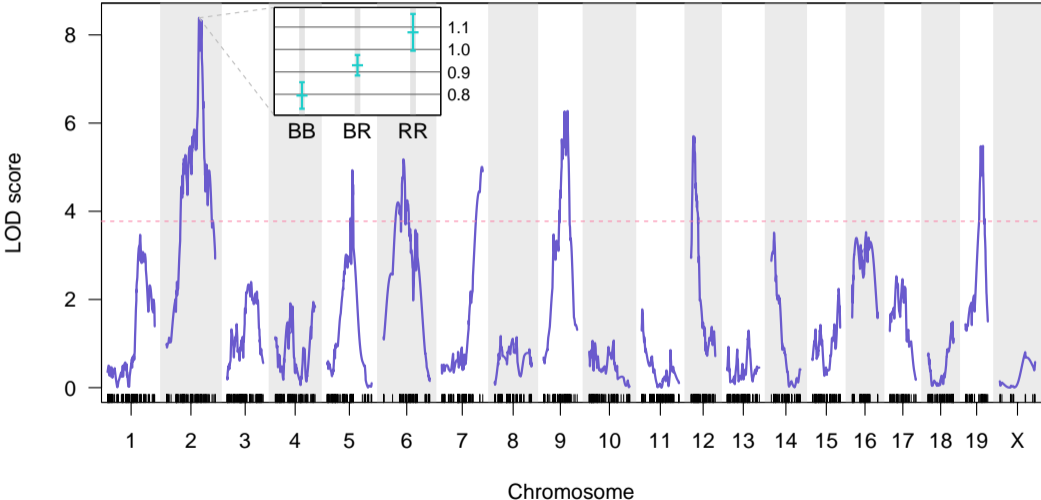
Data



Genome scan



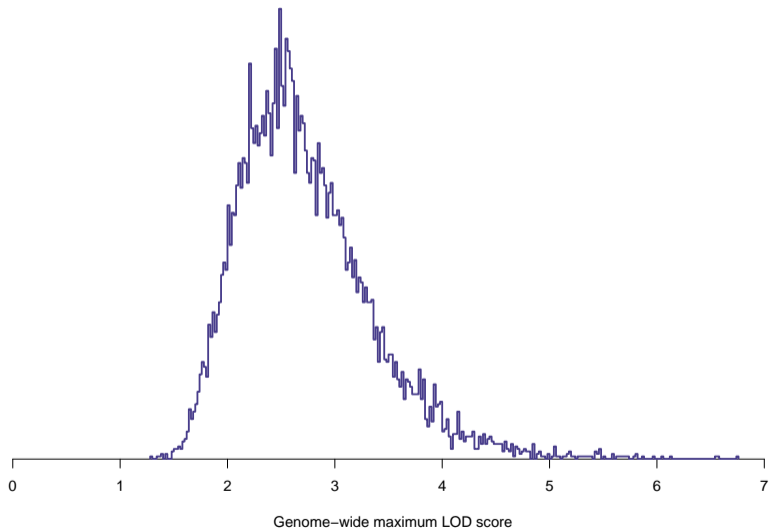
Genome scan



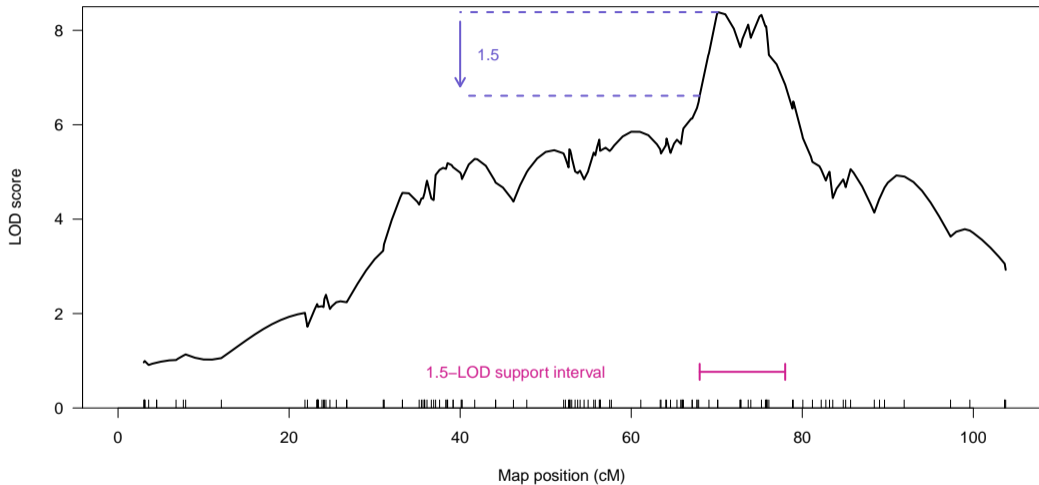
Permutation test



Permutation distribution



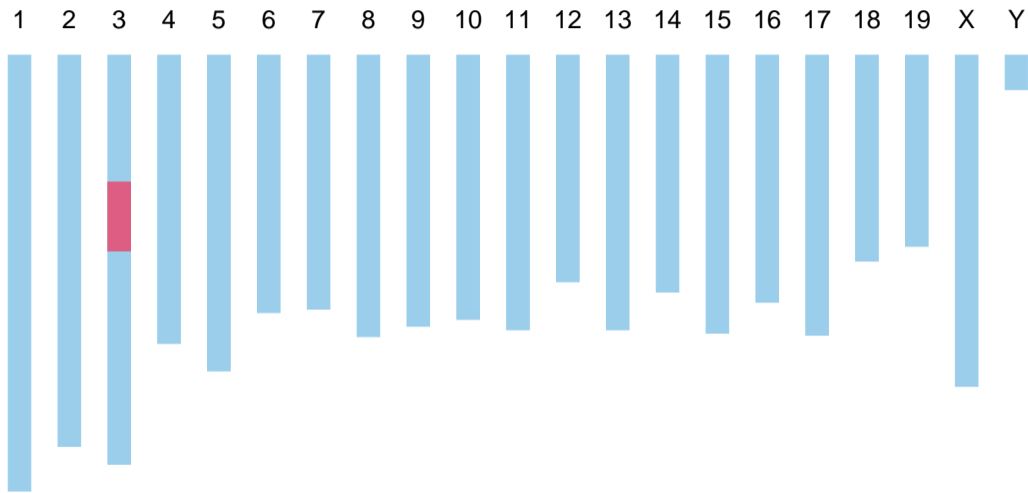
QTL intervals



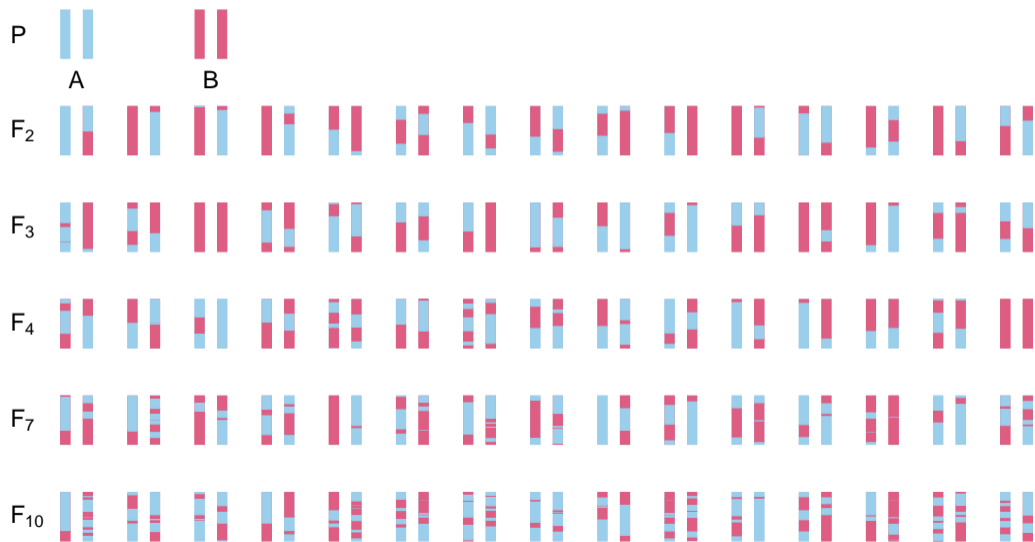
Multiple QTL models

- ▶ Reduce residual variation \rightarrow greater power
- ▶ Separate linked QTL
- ▶ Identify interactions (epistasis)

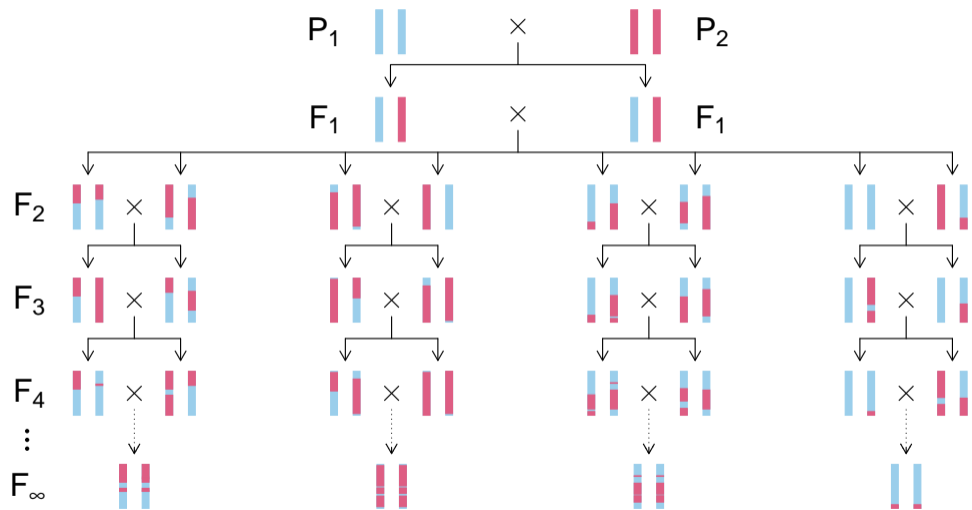
Congenic line



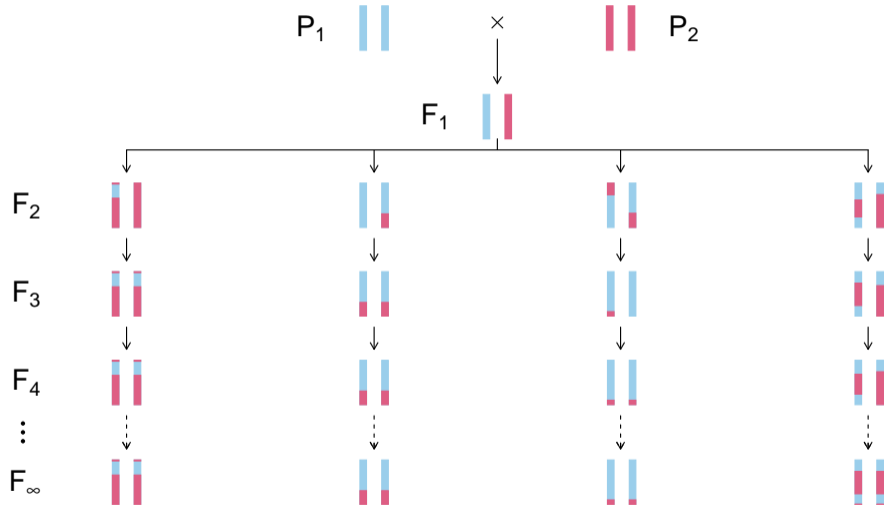
Advanced intercross lines



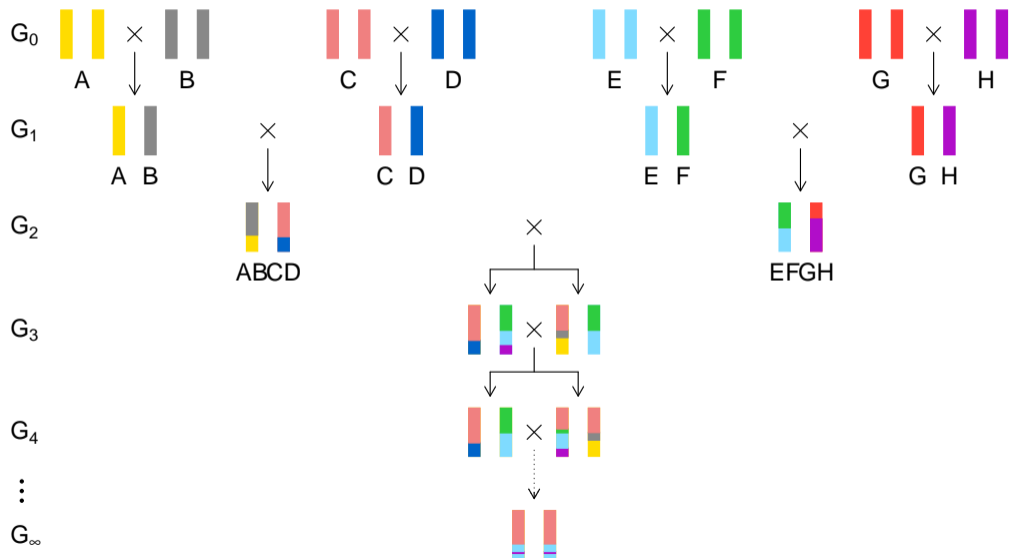
Recombinant inbred lines



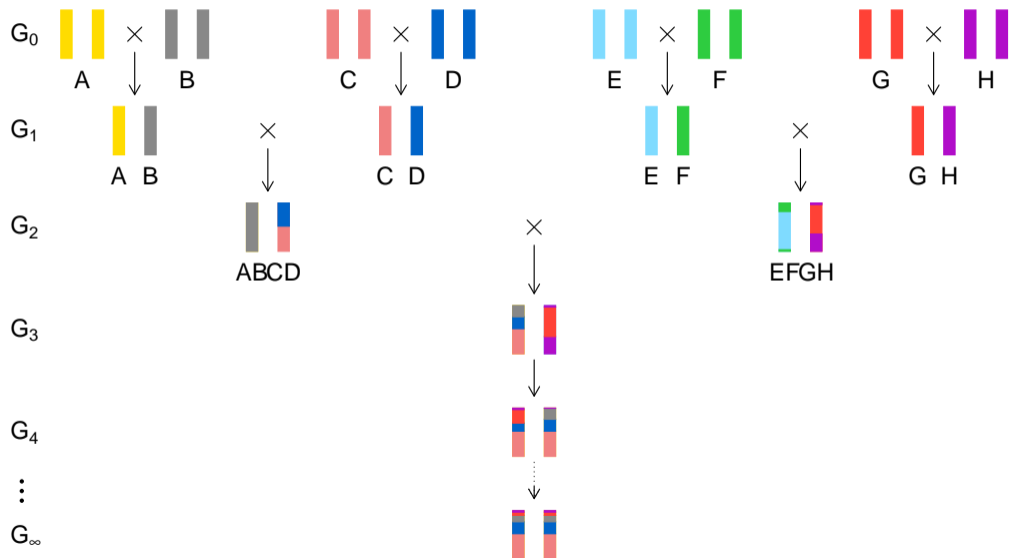
Recombinant inbred lines (selfing)



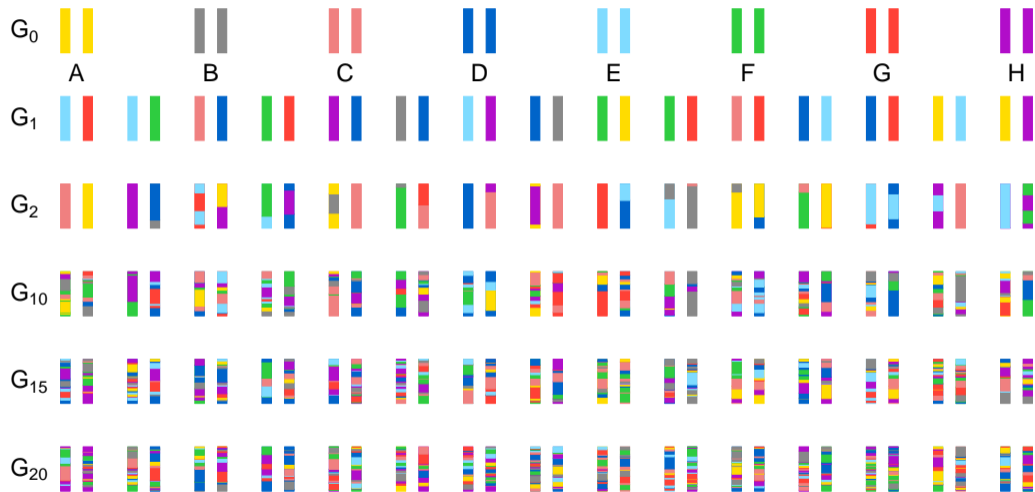
Collaborative Cross



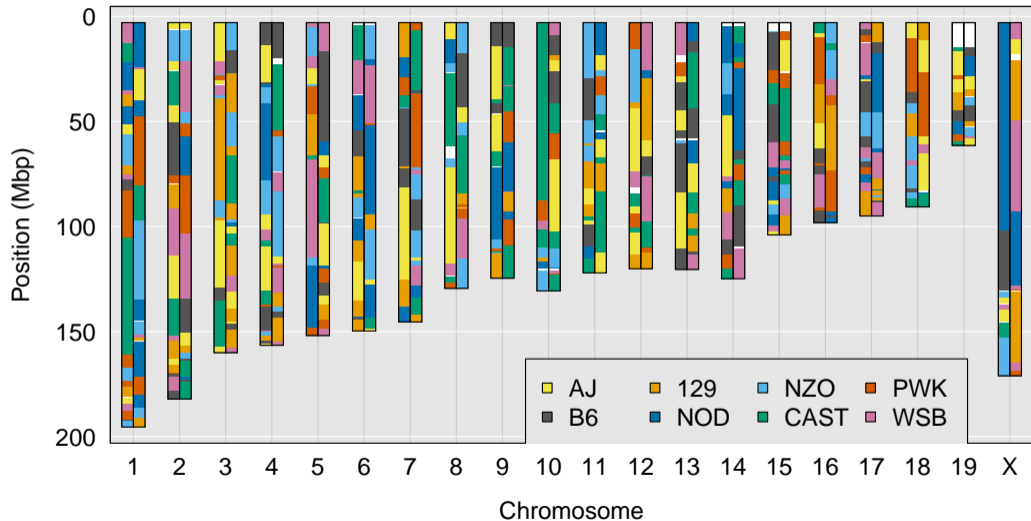
MAGIC lines



Heterogeneous Stock/Diversity outbreeds



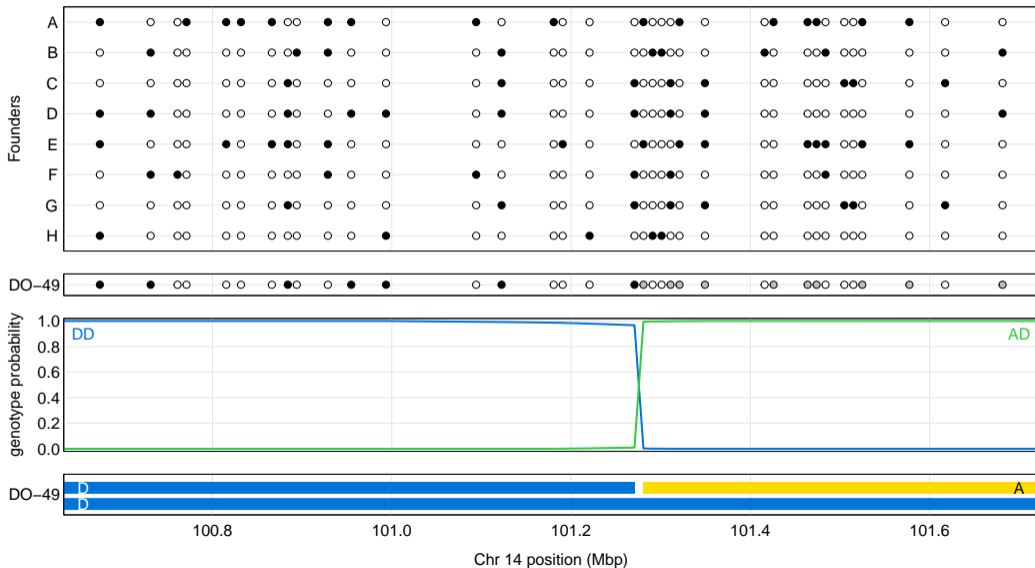
DO genome



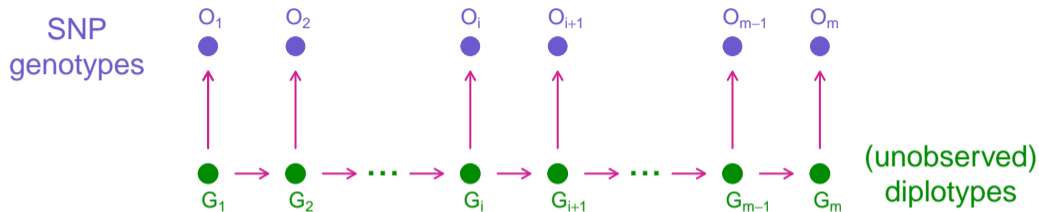
QTL analysis in DO

- ▶ Genotype reconstruction
- ▶ Treatment of QTL genotype
- ▶ Kinship correction

Genotype reconstruction



Hidden Markov model

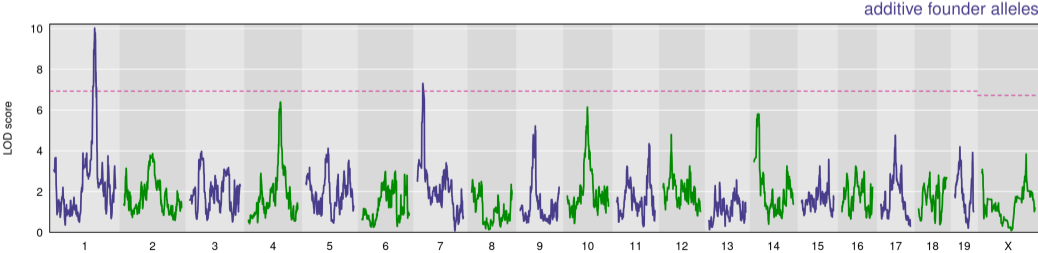
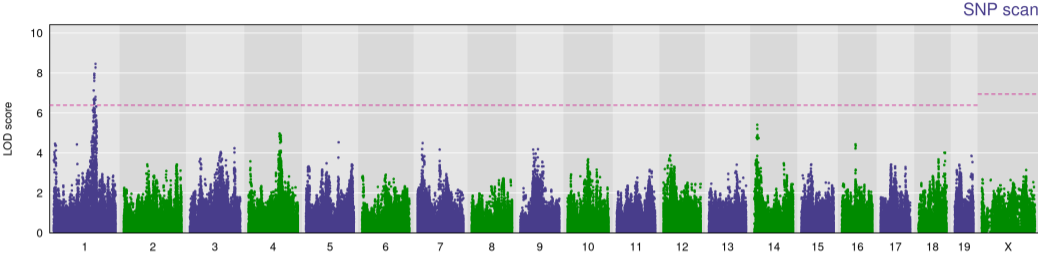


Initial $\pi(g) = \Pr(G_1 = g)$

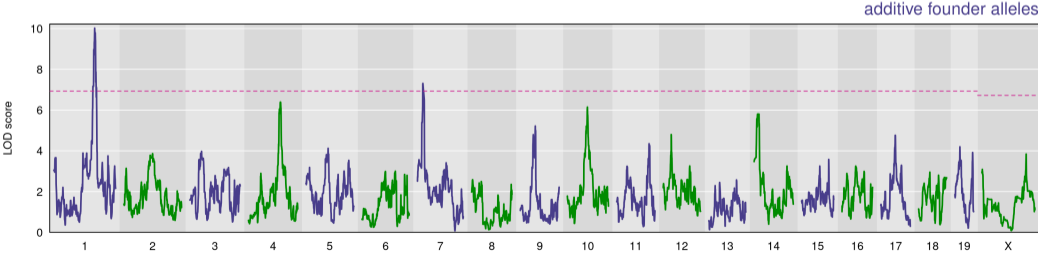
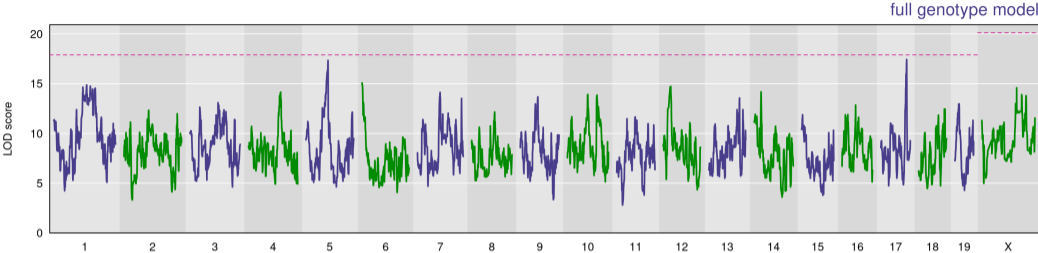
Transition $t_i(g, g') = \Pr(G_{i+1} = g' \mid G_i = g)$

Emission $e_i(g) = \Pr(O_i \mid G_i = g)$

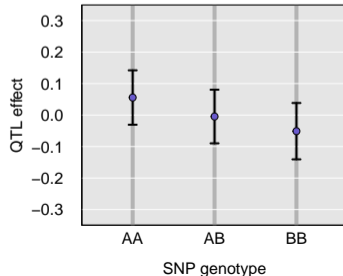
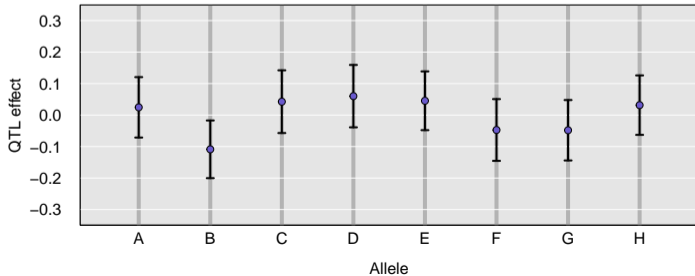
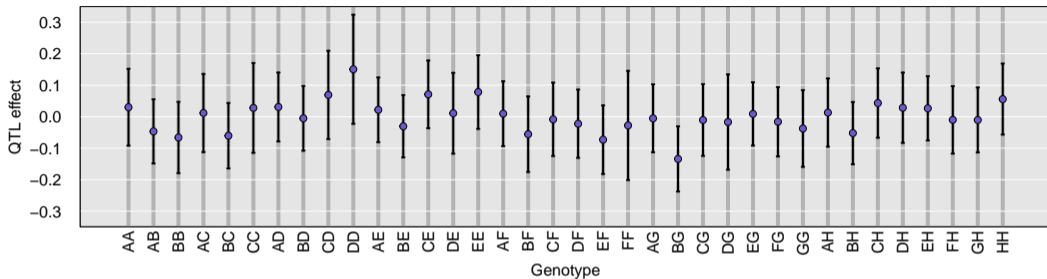
Treatment of QTL genotypes



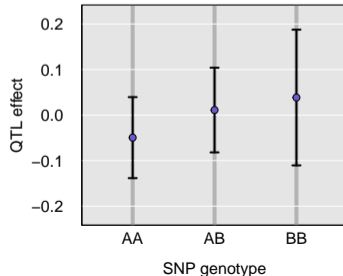
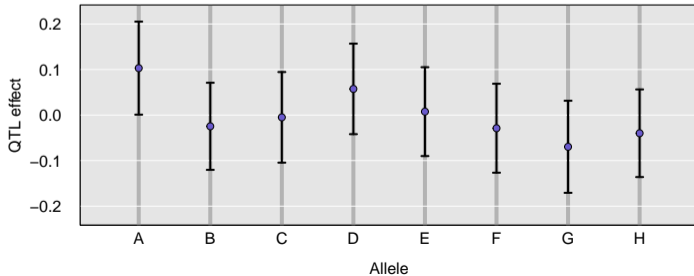
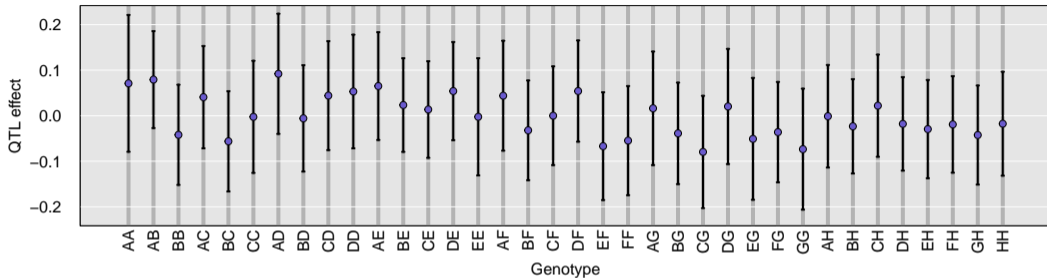
Treatment of QTL genotypes



QTL effects (chr 1)



QTL effects (chr 7)



Linear mixed model

$$y_i = \mu + \sum_k \beta_k q_{ik} + \epsilon_i \quad \epsilon_i \sim \mathbf{N}(0, \sigma_e^2)$$

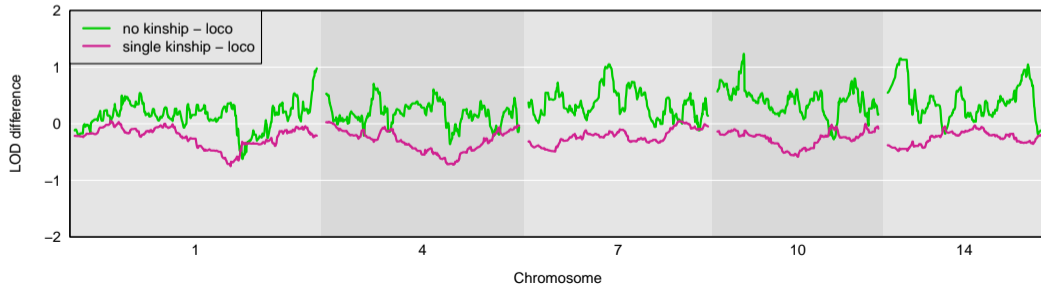
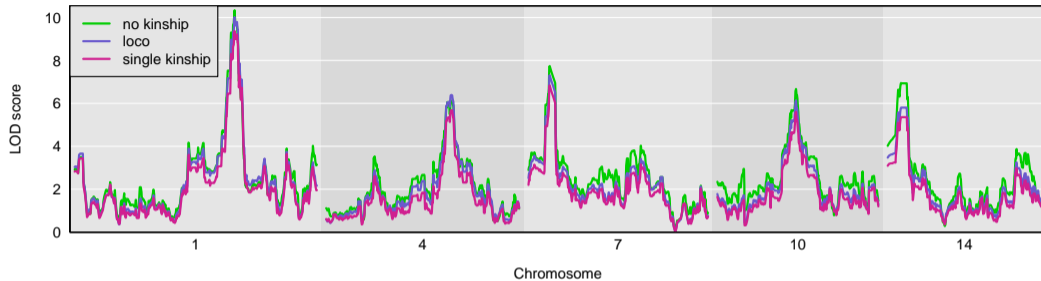
$$= \mu + \eta_i + \epsilon_i \quad \eta_i \sim \mathbf{N}(0, \sigma_p^2)$$

$$\text{cov}(\eta_i, \eta_j) = \sigma_p^2 (2k_{ij})$$

Kinship and LOCO

- ▶ kinship coefficient measures similarity of two individuals' genomes
- ▶ generally estimated from genotype data
- ▶ generally using the “leave one chromosome out (loco)” method
 - Estimate kinship using all chromosomes except the one being scanned

LM vs LMM vs LOCO



Research topics

- ▶ Identifying the causal polymorphisms
- ▶ Joint analysis of high-dimensional outcomes
- ▶ Use of intermediate biochemical traits
- ▶ Cross-species analyses
- ▶ QTL \times QTL interactions (epistasis)
- ▶ QTL \times covariate interactions (e.g. sex, diet, or environment)

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