QTL mapping with -omics scale data

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Plant Developmental Biology
2015_02_18

Lecture Outline

- What is a QTL?
- Successful QTL mapping examples
- Single Marker Regression
- Simple Interval Mapping
- Multi-QTL models
- Genome Wide Data- How do we scale?
- Expression QTL (eQTL)
- Integrating eQTL with other QTL for candidate gene identification

What is a QTL?

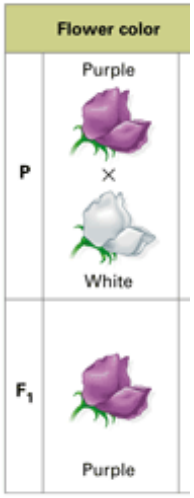
- Quantitative Trait Loci
- A genetic locus that contributes to <u>quantitative</u> variation in a <u>trait</u>

- Simple discrete traits vs. continuous traits

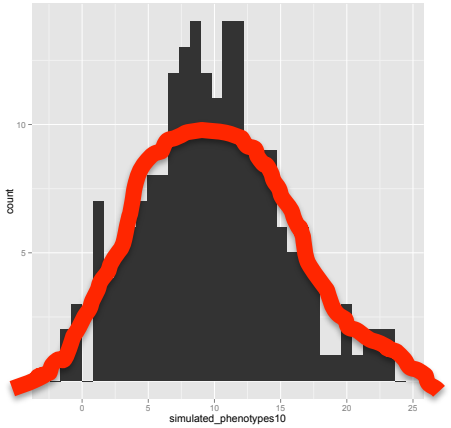
-number of genes involved

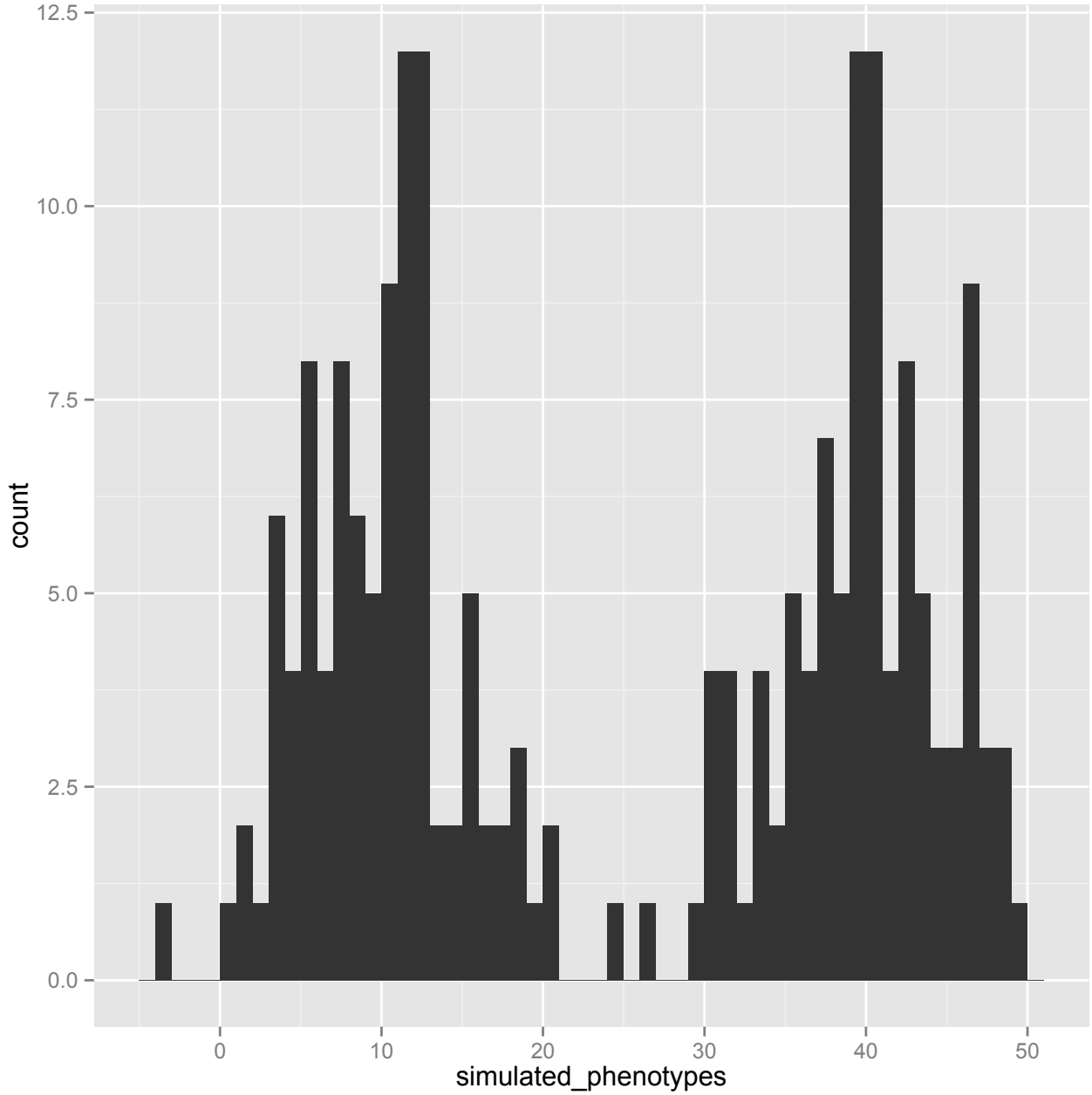
-environmental effects

-genetic background



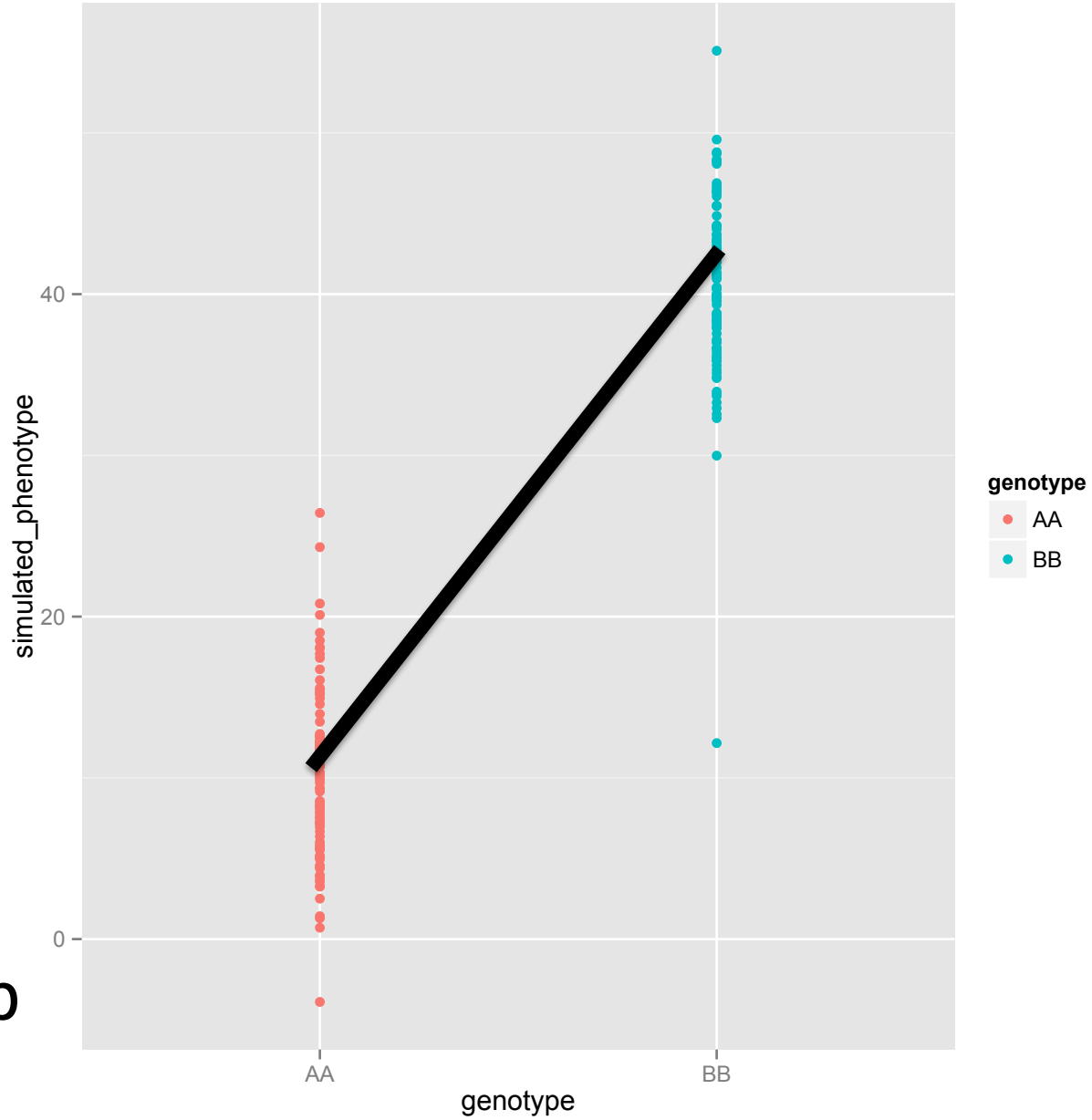
vs.





Mean = 10

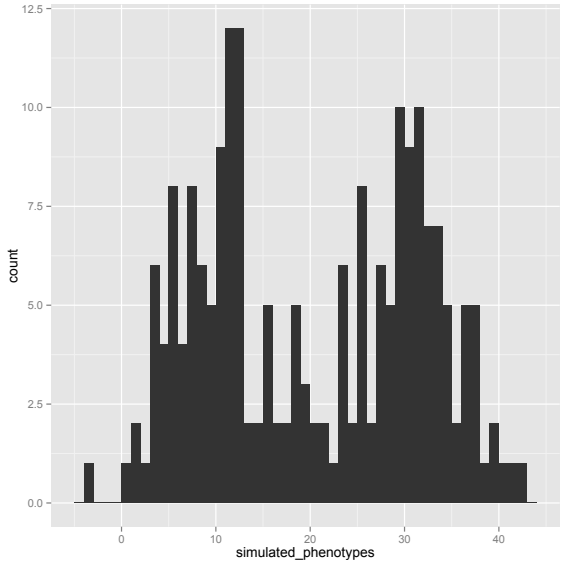
Mean = 40

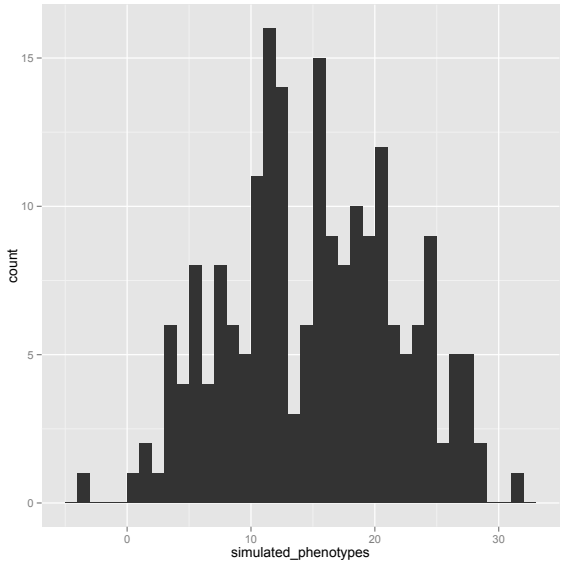


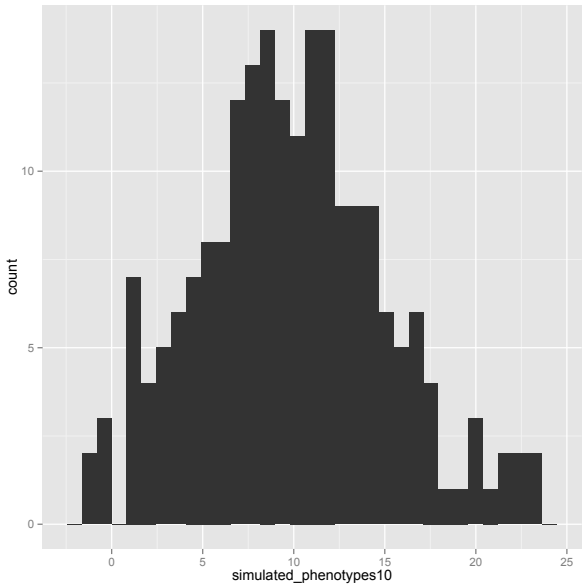
$y = mx + b$

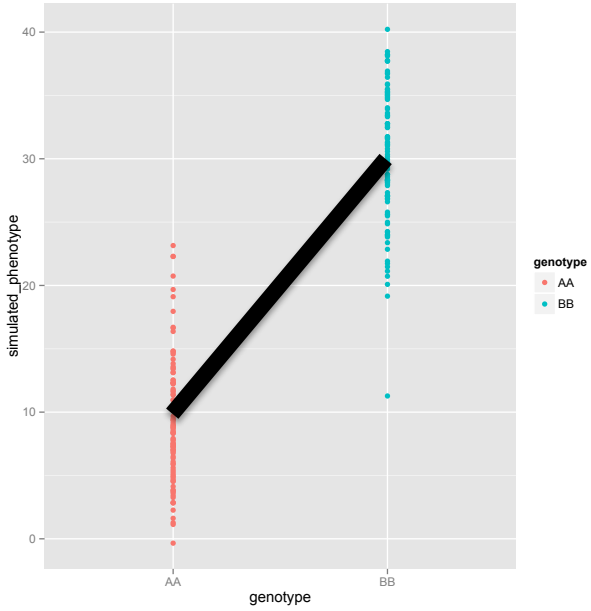
$phenotype = m*gtBB + mean + error$

Given genotype, is slope different from 0?

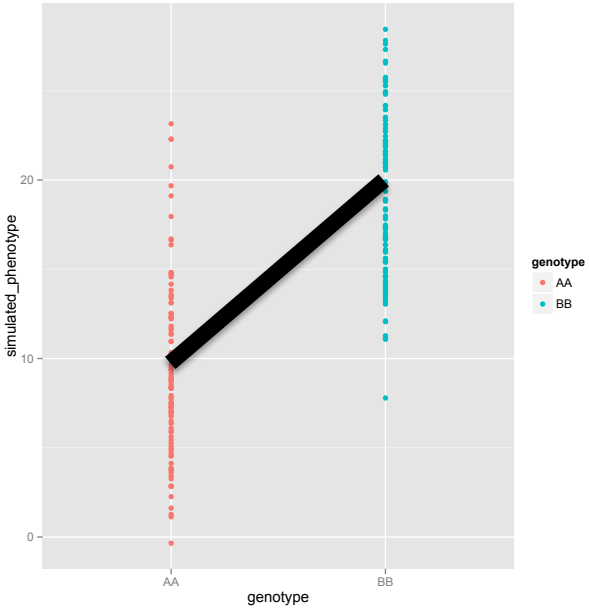








10 30



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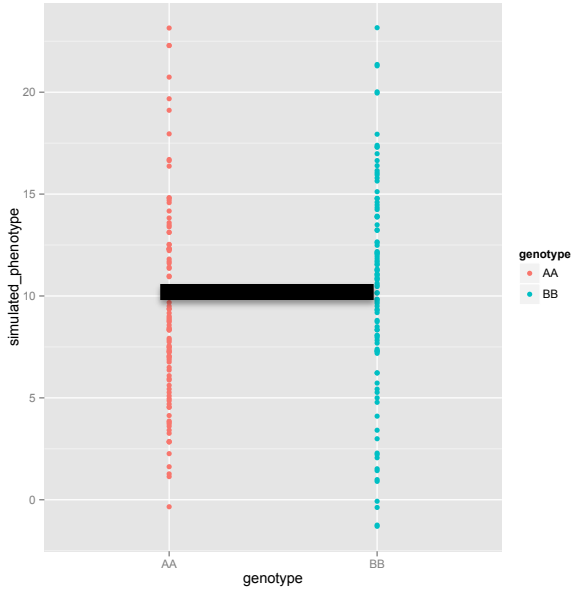

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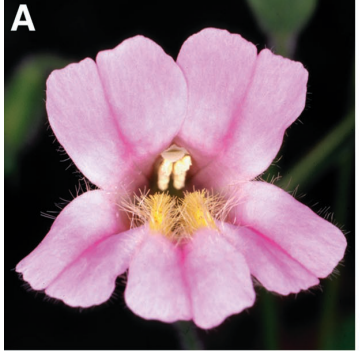
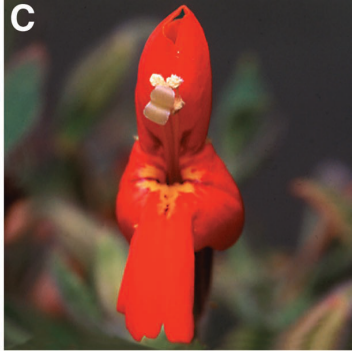


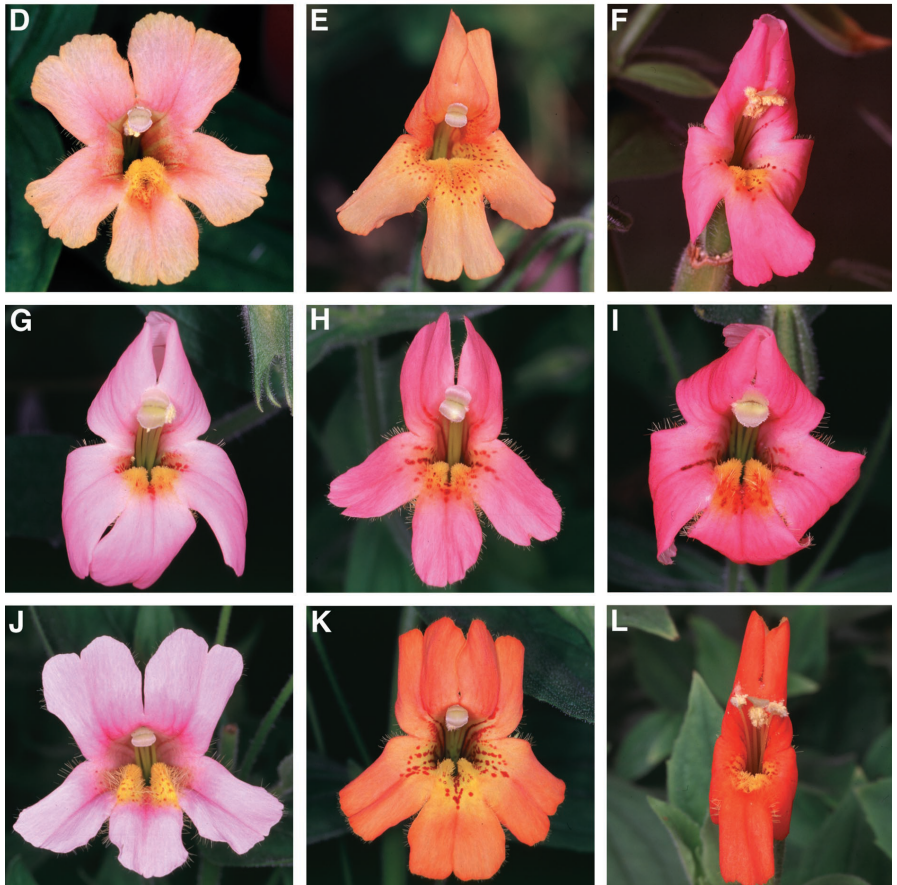
M. lewisii

F1



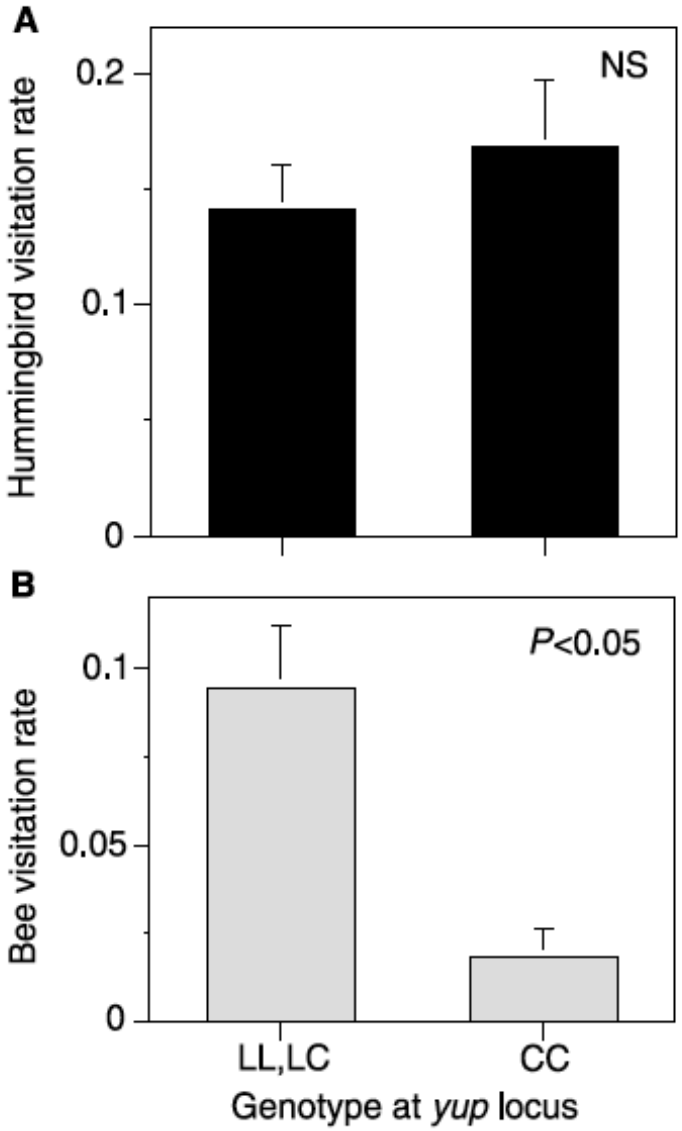
M. cardinalis

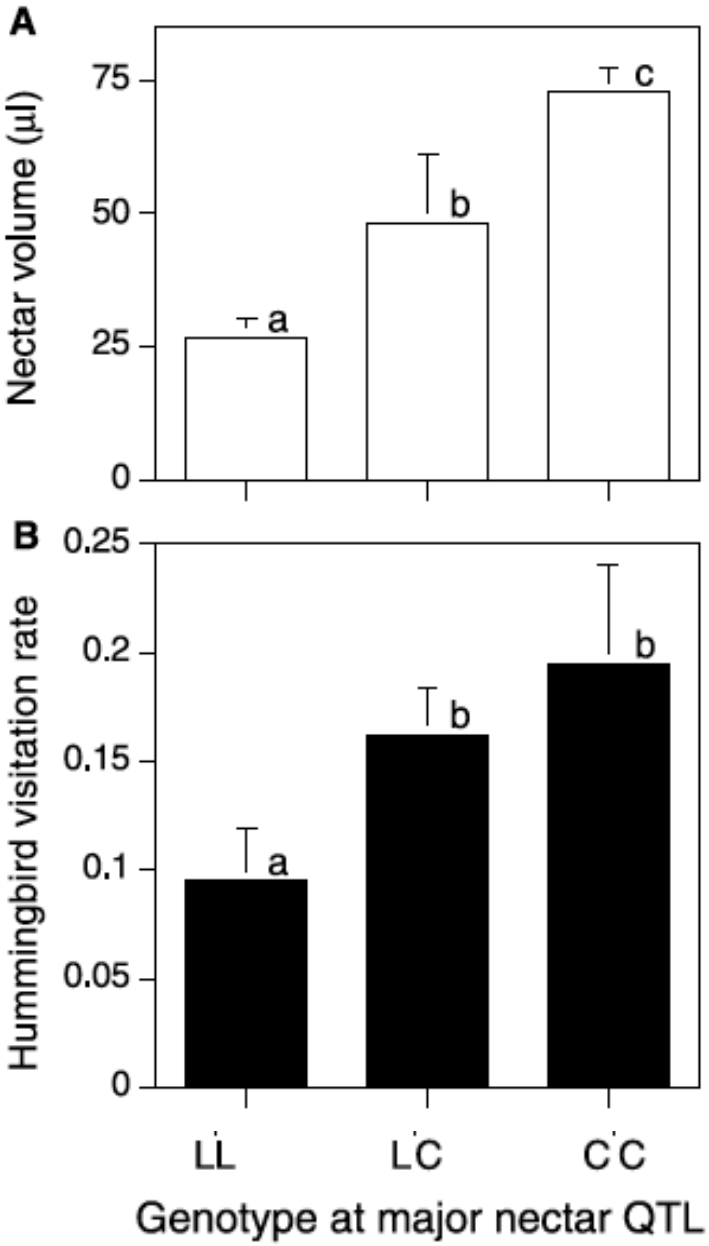
Schemske and
Bradshaw
PNAS 1999



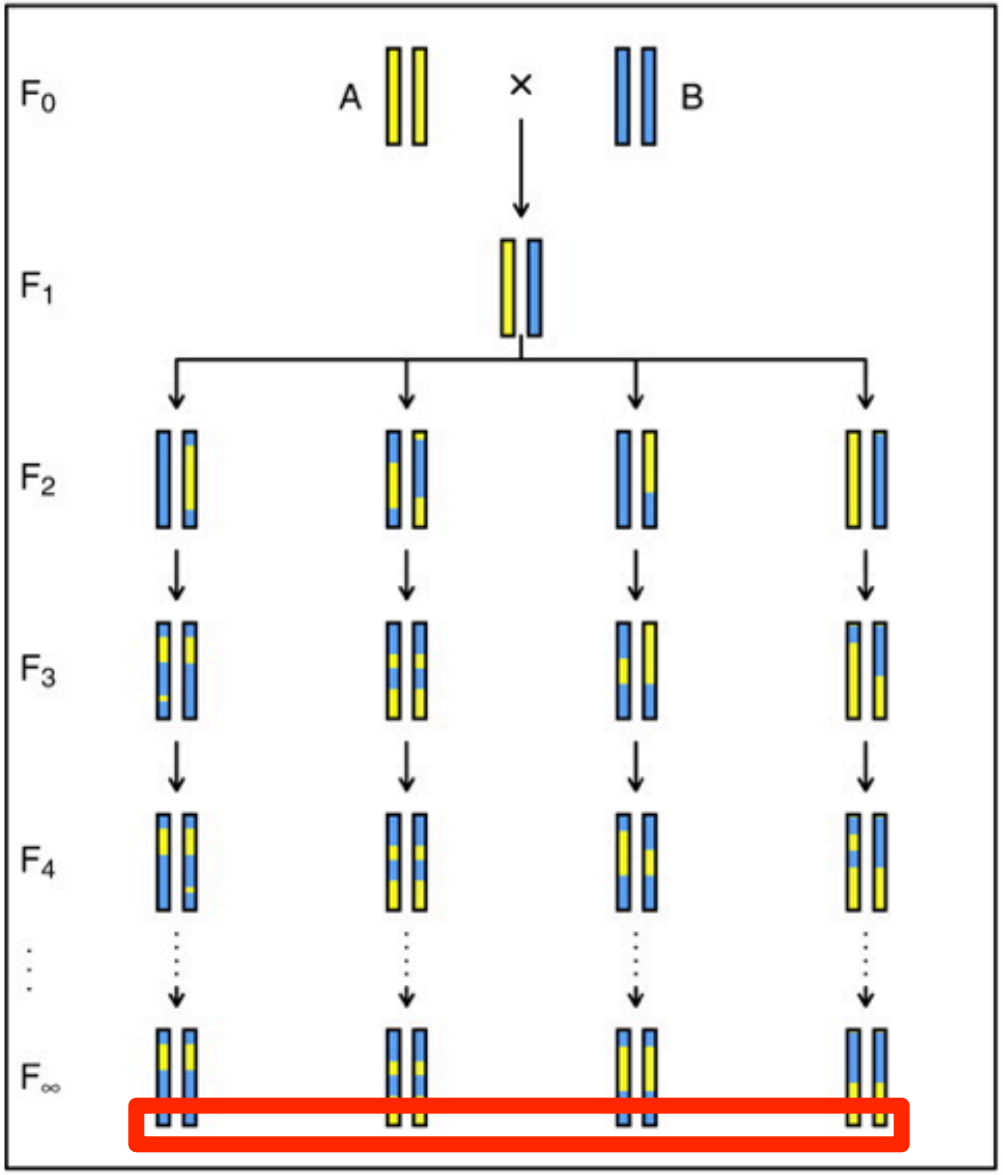
F2

Flower phenotype QTL alter pollinator visits!



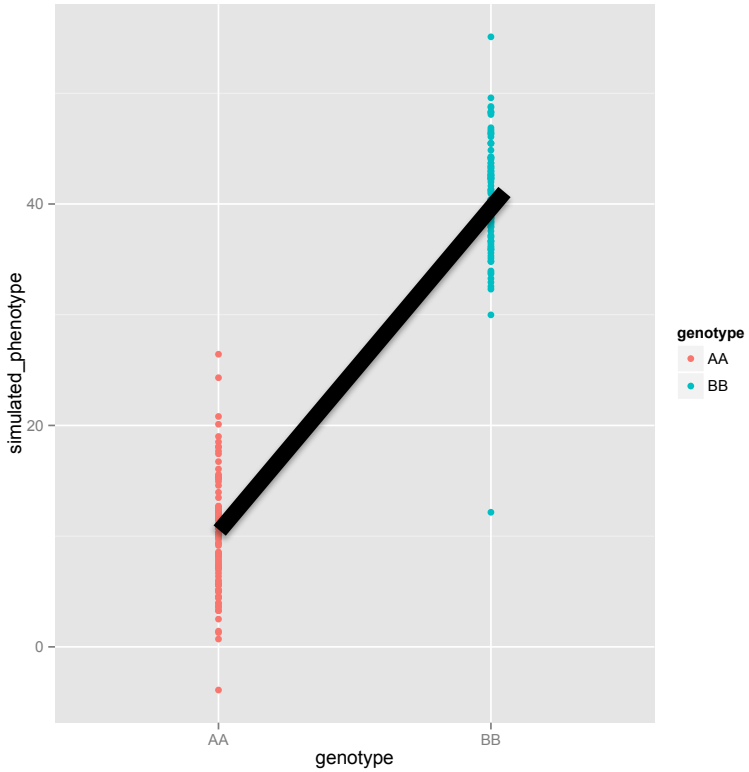


Recombinant Inbred Lines (RILs)



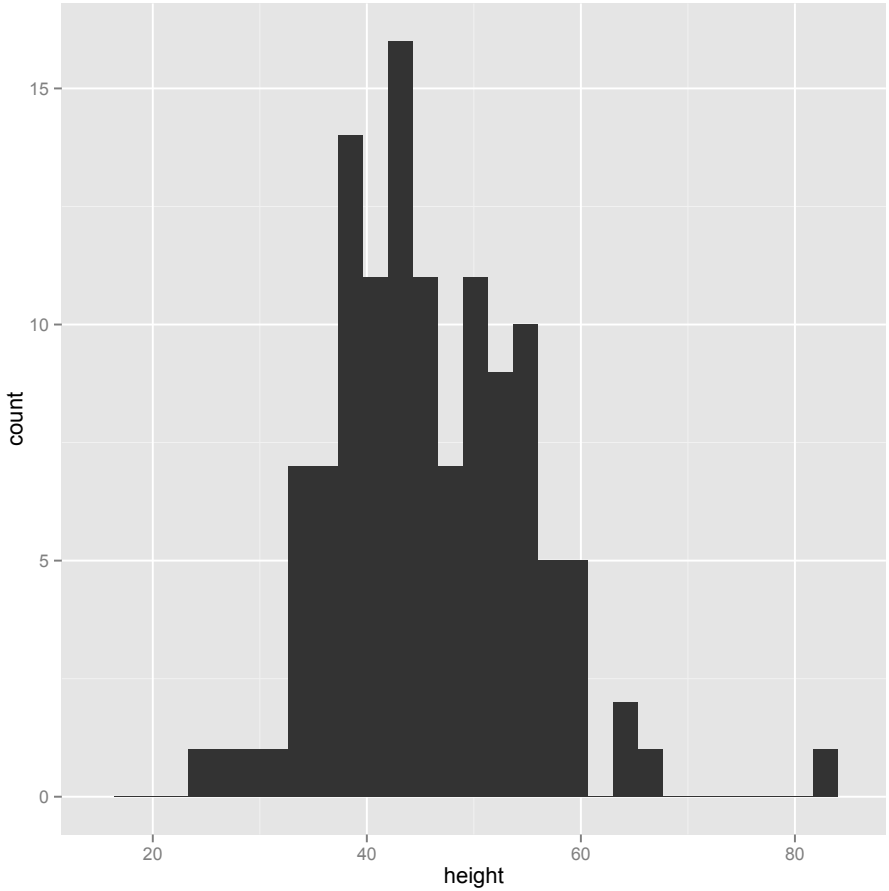
Marker Regression

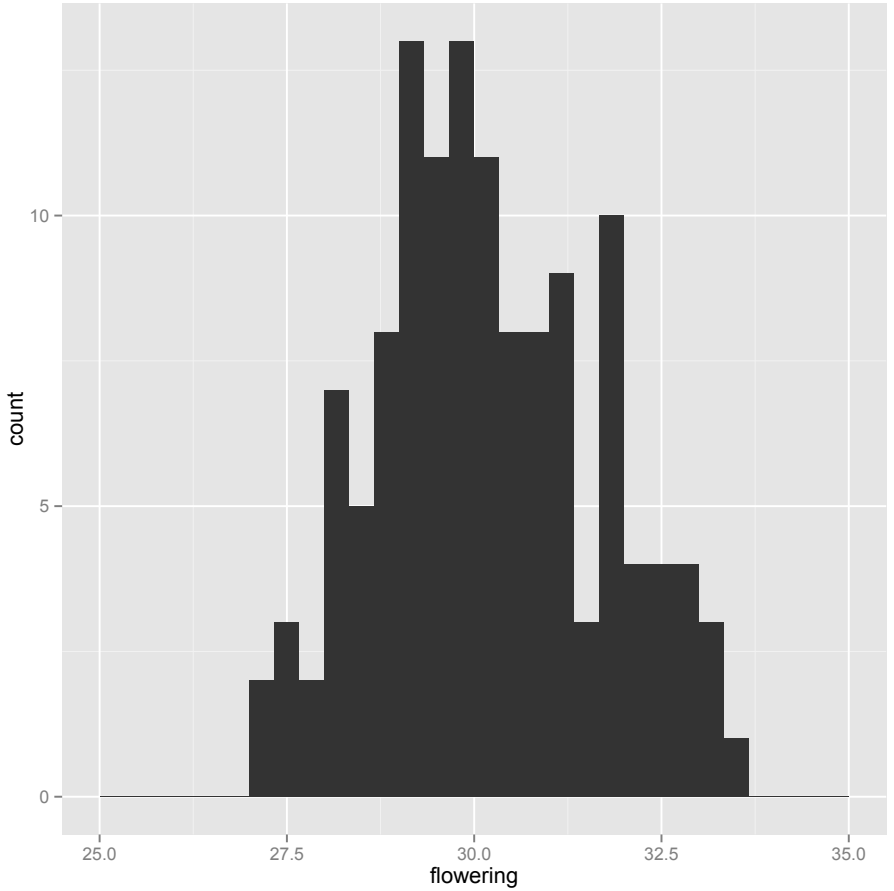
Chr A10



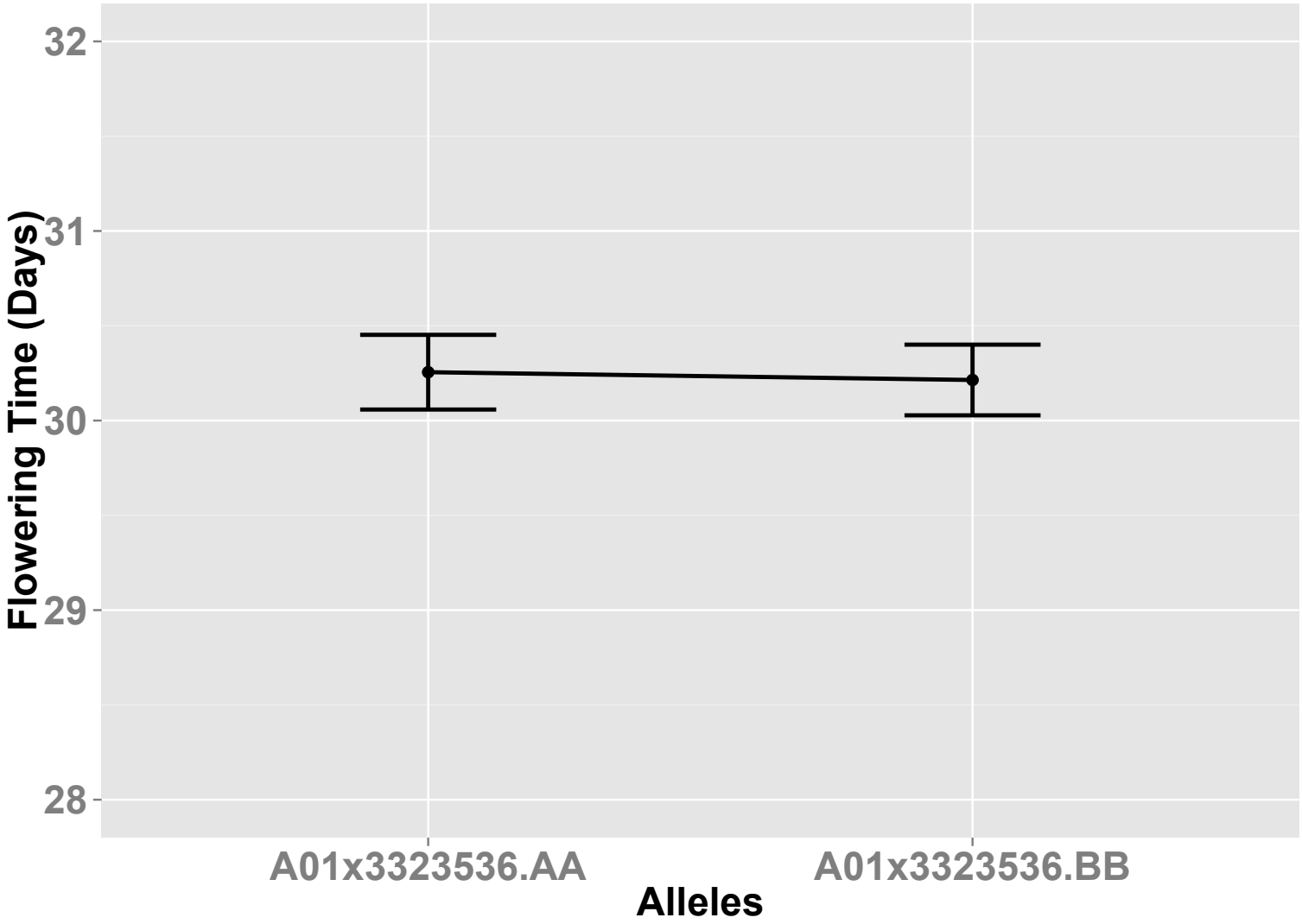
phenotype = m*gtBB + mean + error

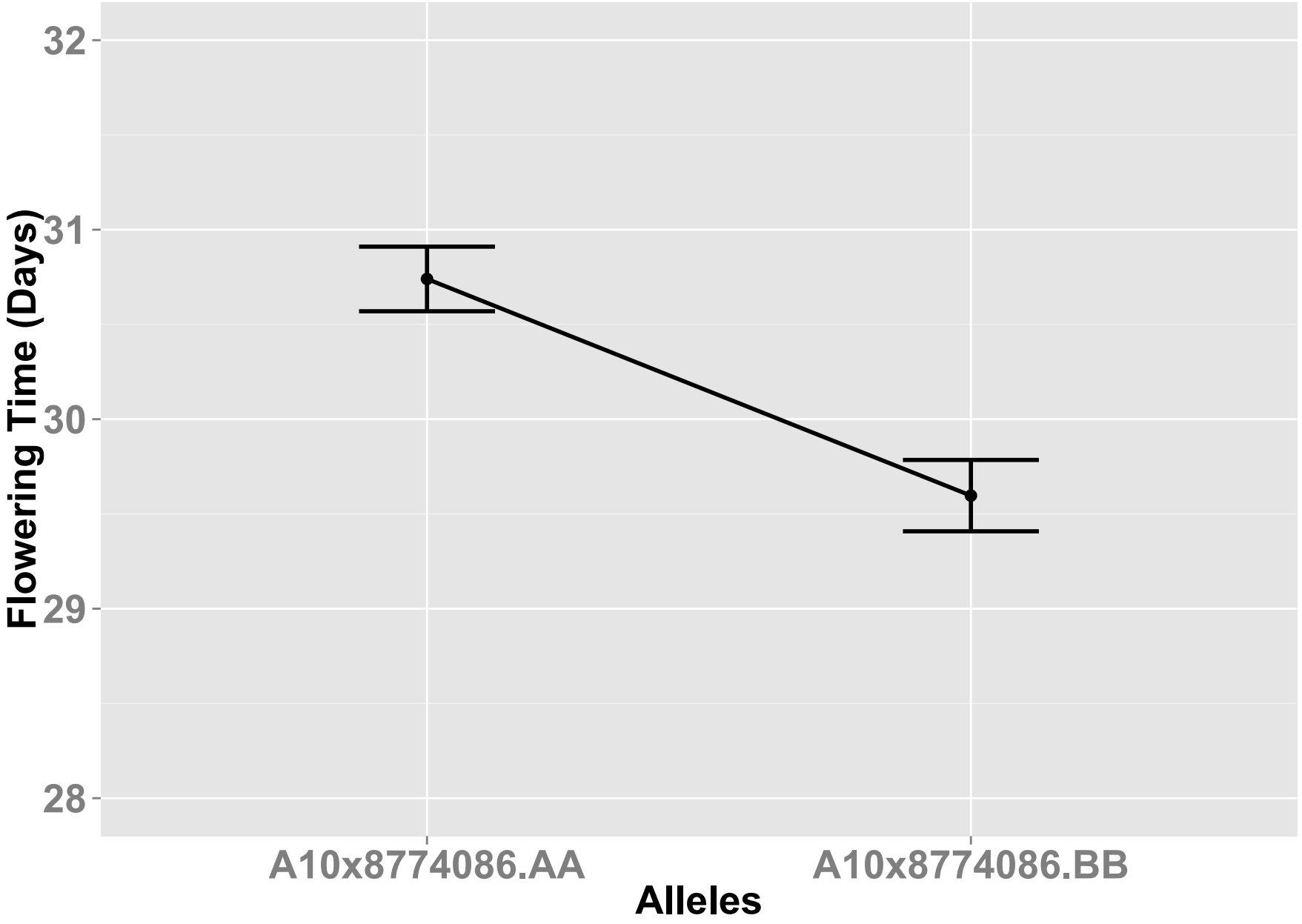
Given genotype, is slope different from 0?



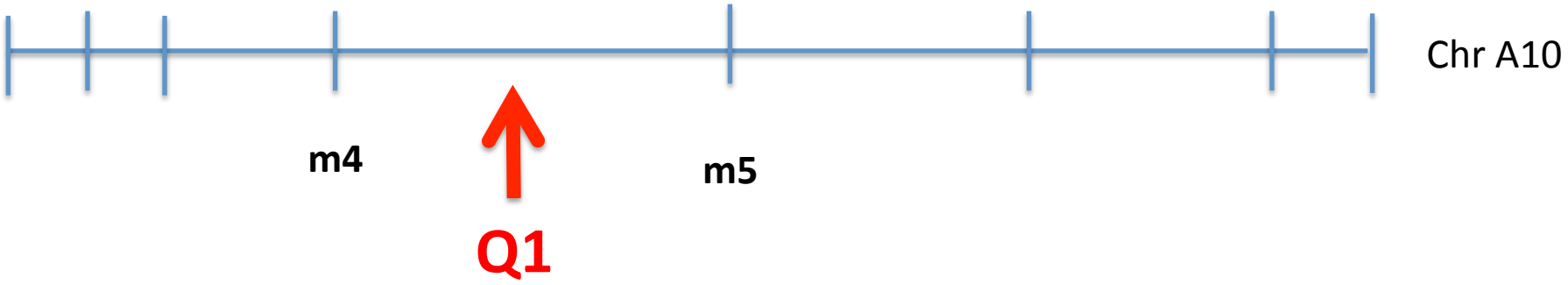


Brassica rapa phenotypic distributions


32
31
30
29
28
Flowering Time (Days)
A01x3323536.AA
A01x3323536.BB
Alleles


32
31
30
29
28
Flowering Time (Days)
A10x8774086.AA
A10x8774086.BB
Alleles

What if QTL is located between known markers?



Solution: Interval Mapping

Evaluate intervals between markers rather than just markers themselves

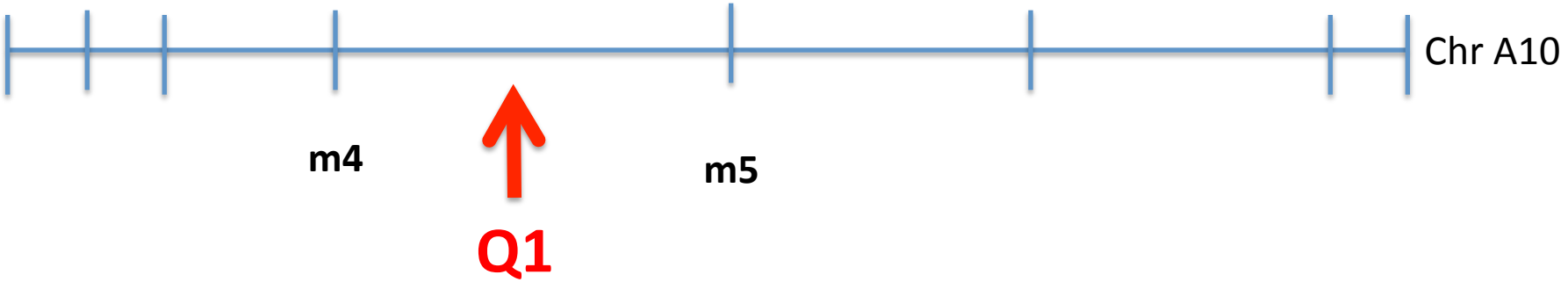
Use known genotypes at flanking markers to determine allelic effect size of QTL

Use recombinants to estimate whether QTL is located closer to marker 4 or marker 5

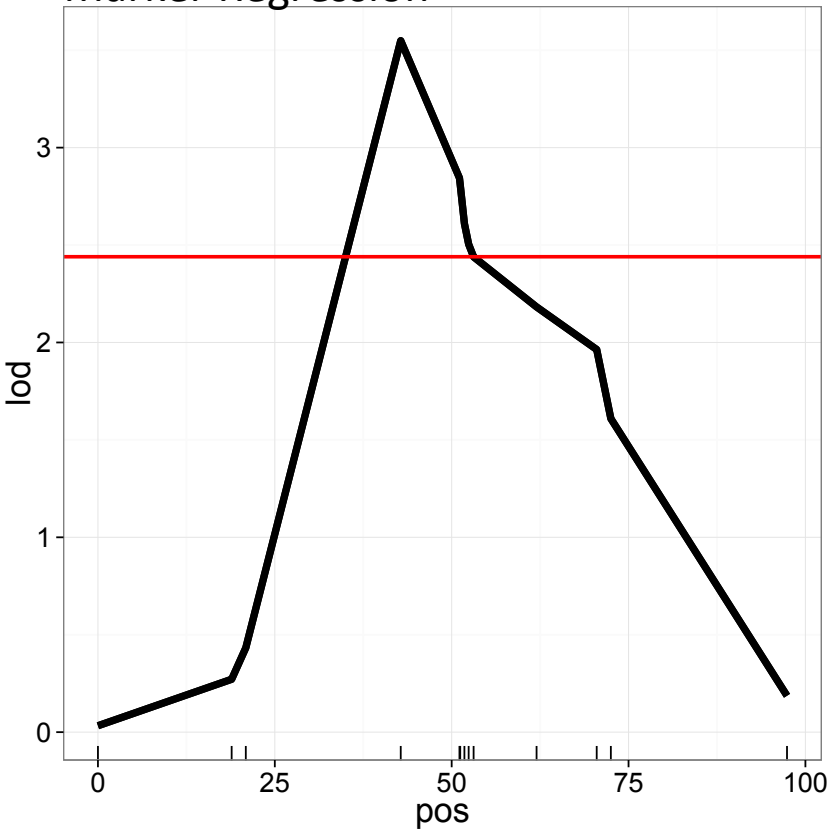
LOD score: Likelihood of linkage.
LOG10(likelihood of linkage/likelihood unlinked)

Compare to null model that there is no QTL anywhere in genome

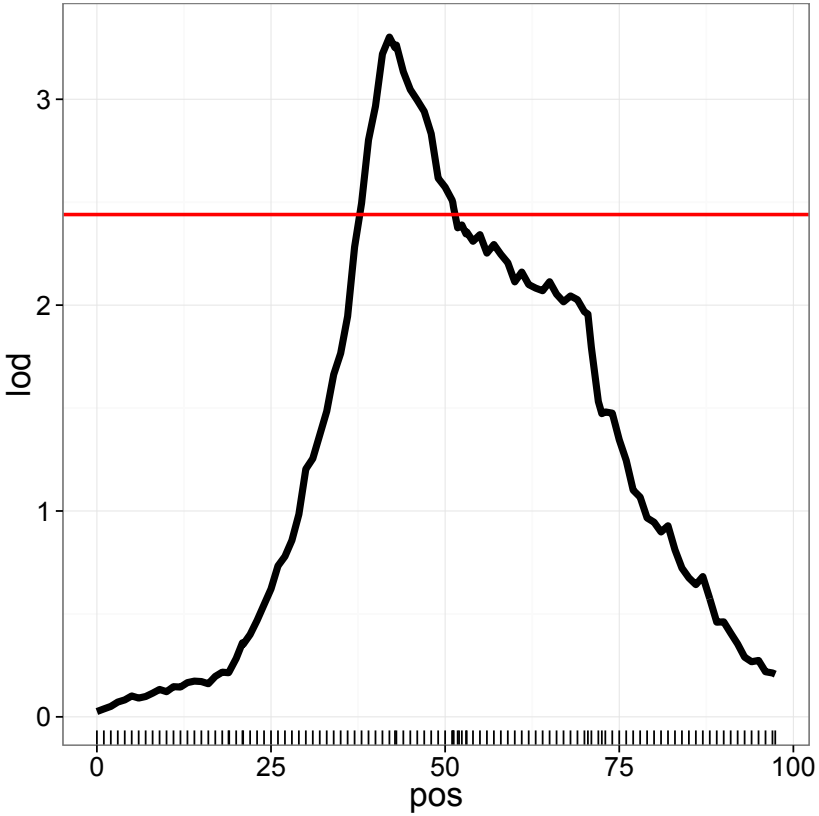
Flowering Time QTL Chromosome A10



Marker Regression

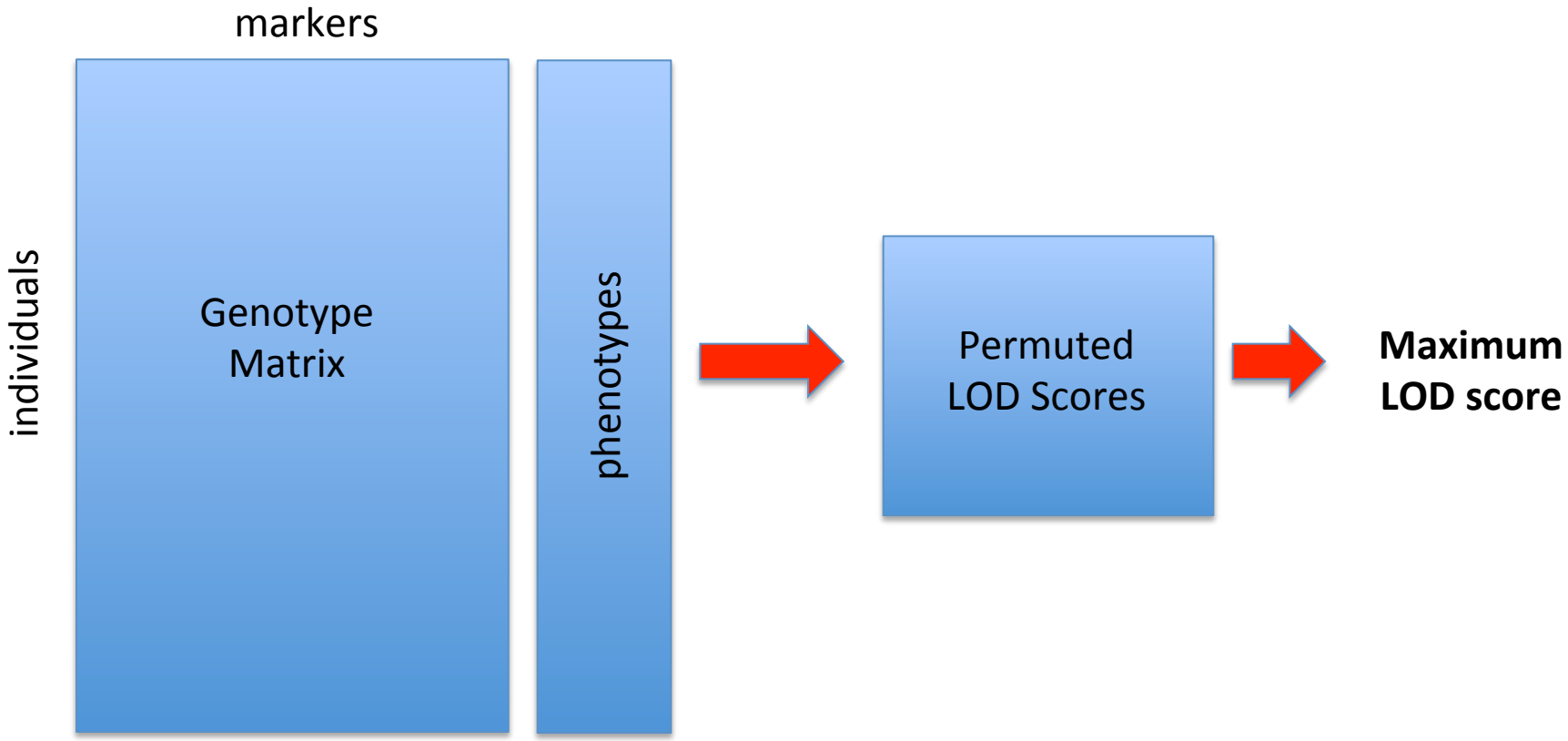


Interval Mapping

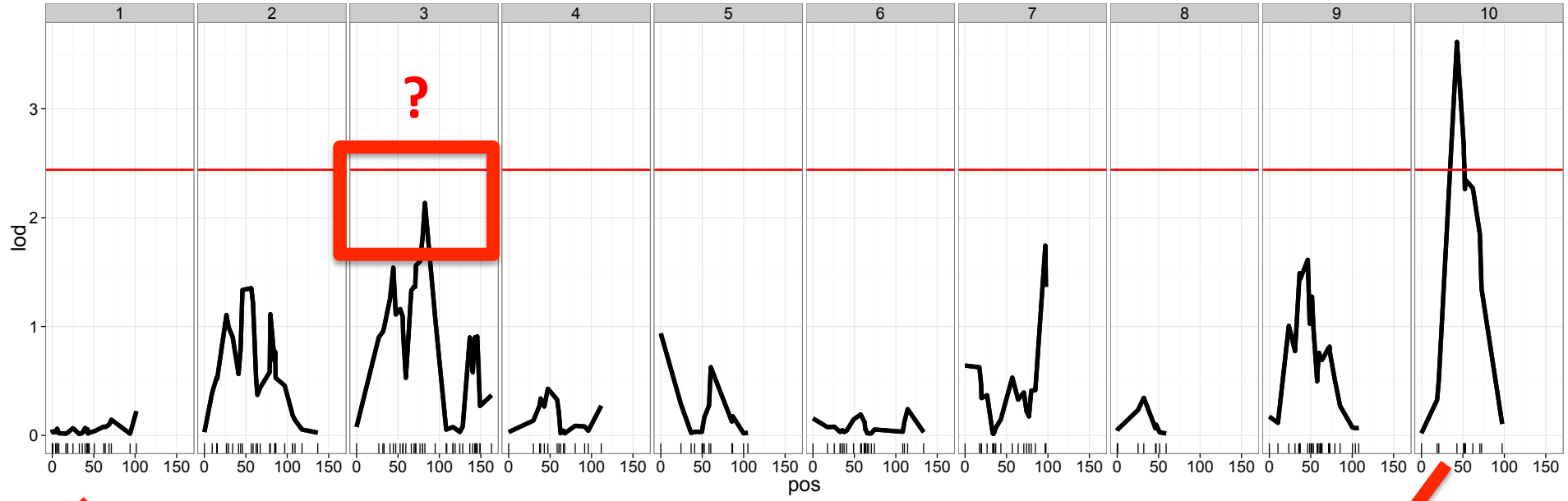


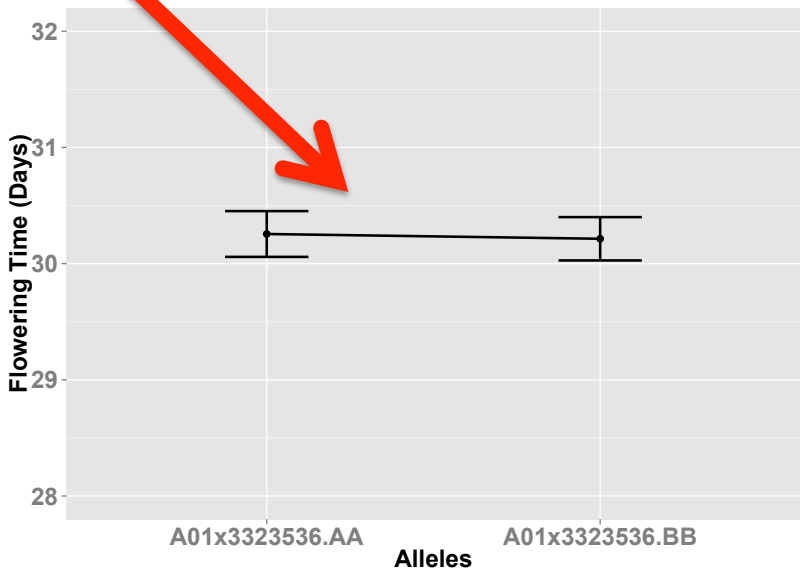
Dense Grid Search for QTL after calculating genotype probabilities
Becomes extremely important for multiple QTL models

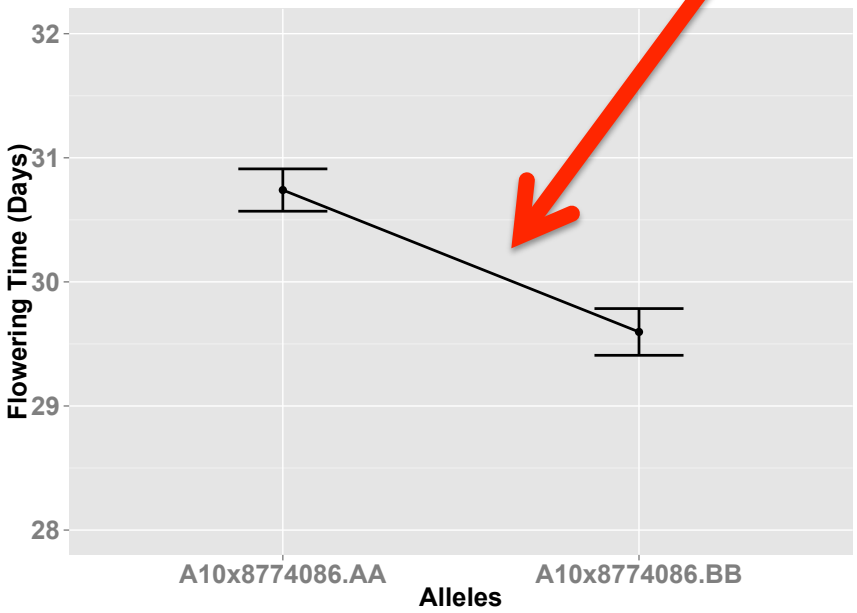
Significance Threshold by permutation tests



Randomly assign phenotypes to genotypes
Calculate genome wide LOD scores
Take maximum LOD score
Repeat 1000x

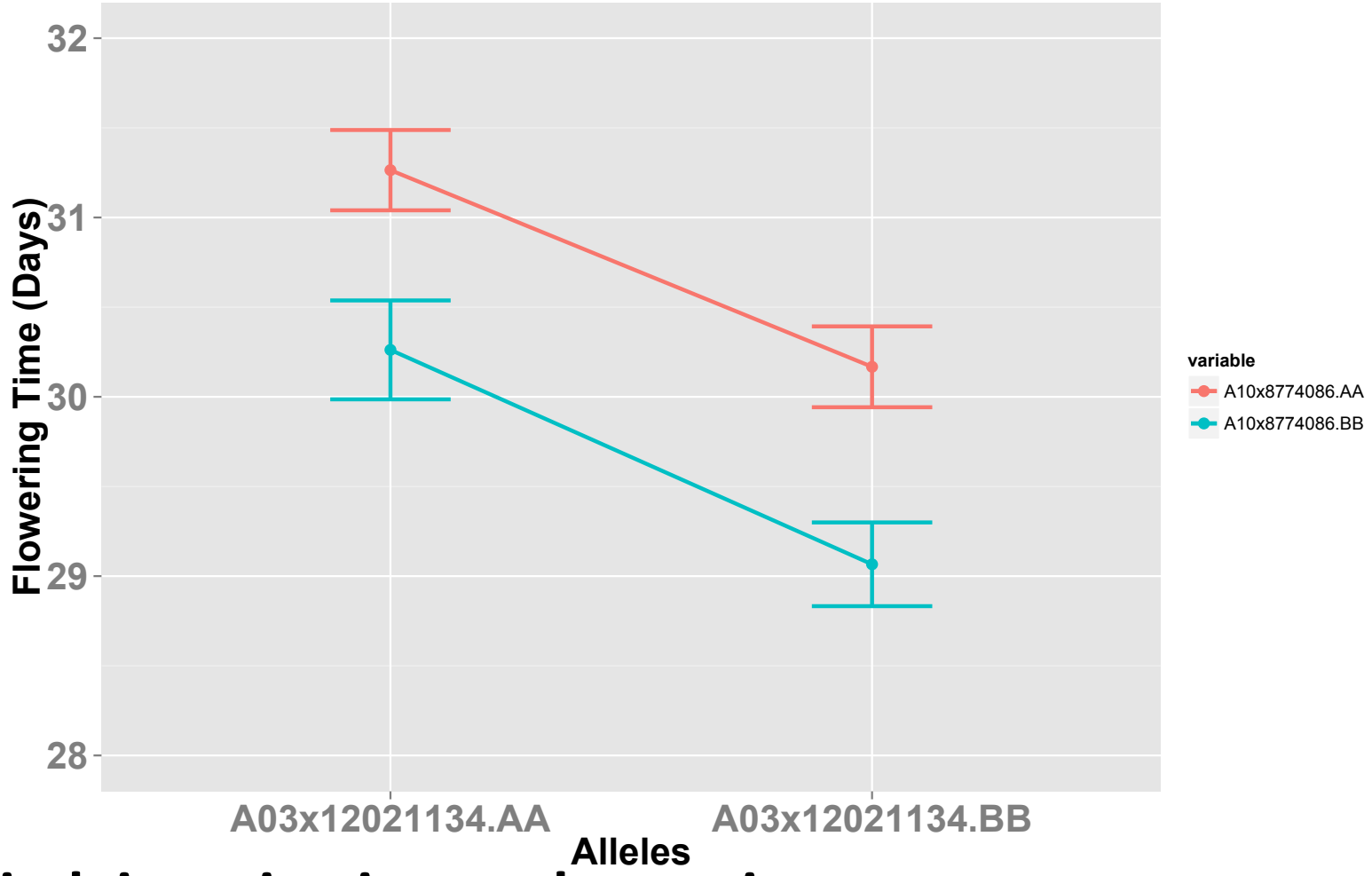






What about multiple QTL explaining trait?

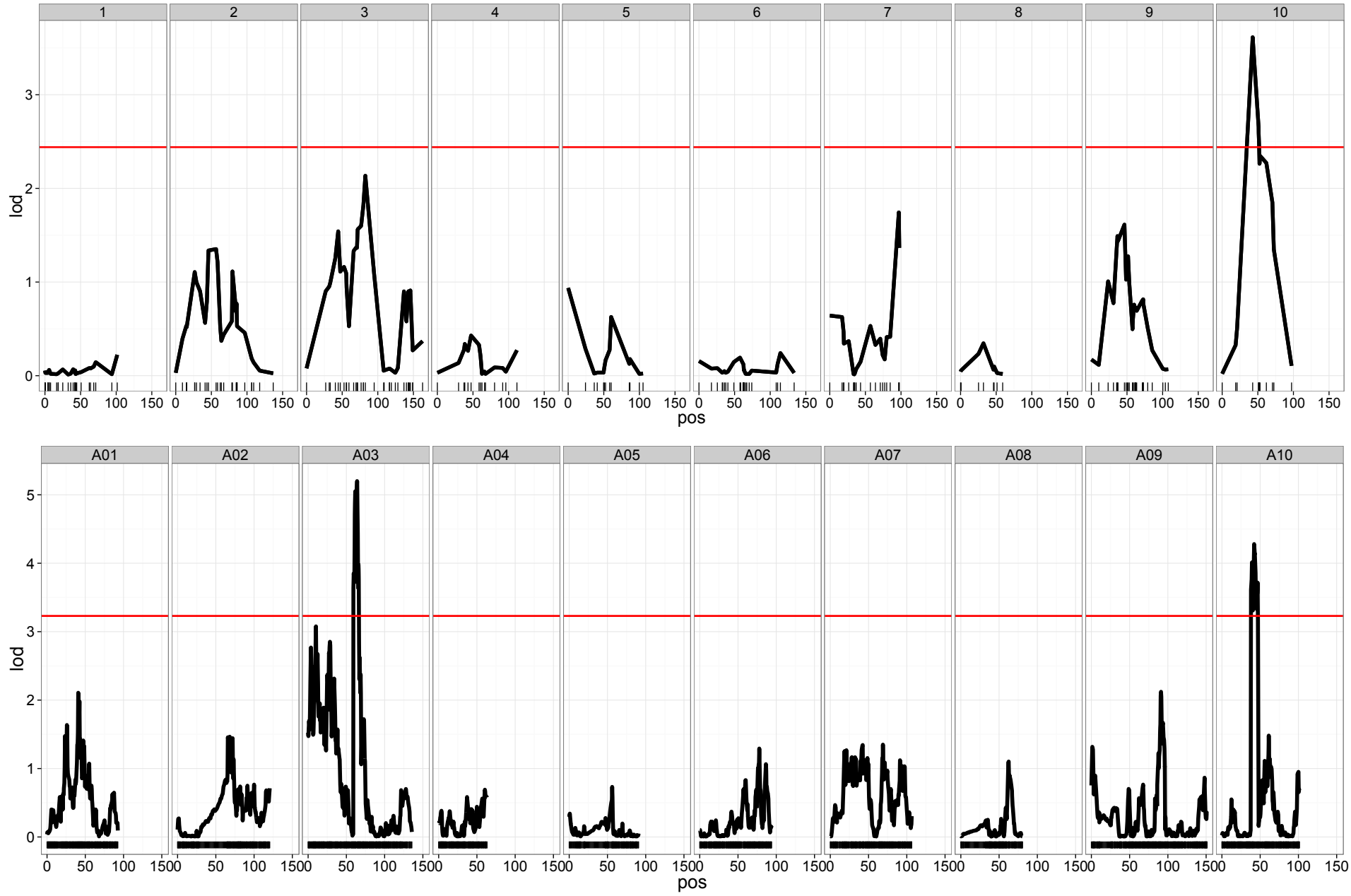
Multi-QTL Models: model selection problem



Simplified, ignoring interval mapping:

phenotype = mean + m1*gtA03_BB + m2*gtA10_BB + error

What if QTL interact? What would this plot look like?



Multiple QTL Models significantly improve fit and narrow QTL peaks

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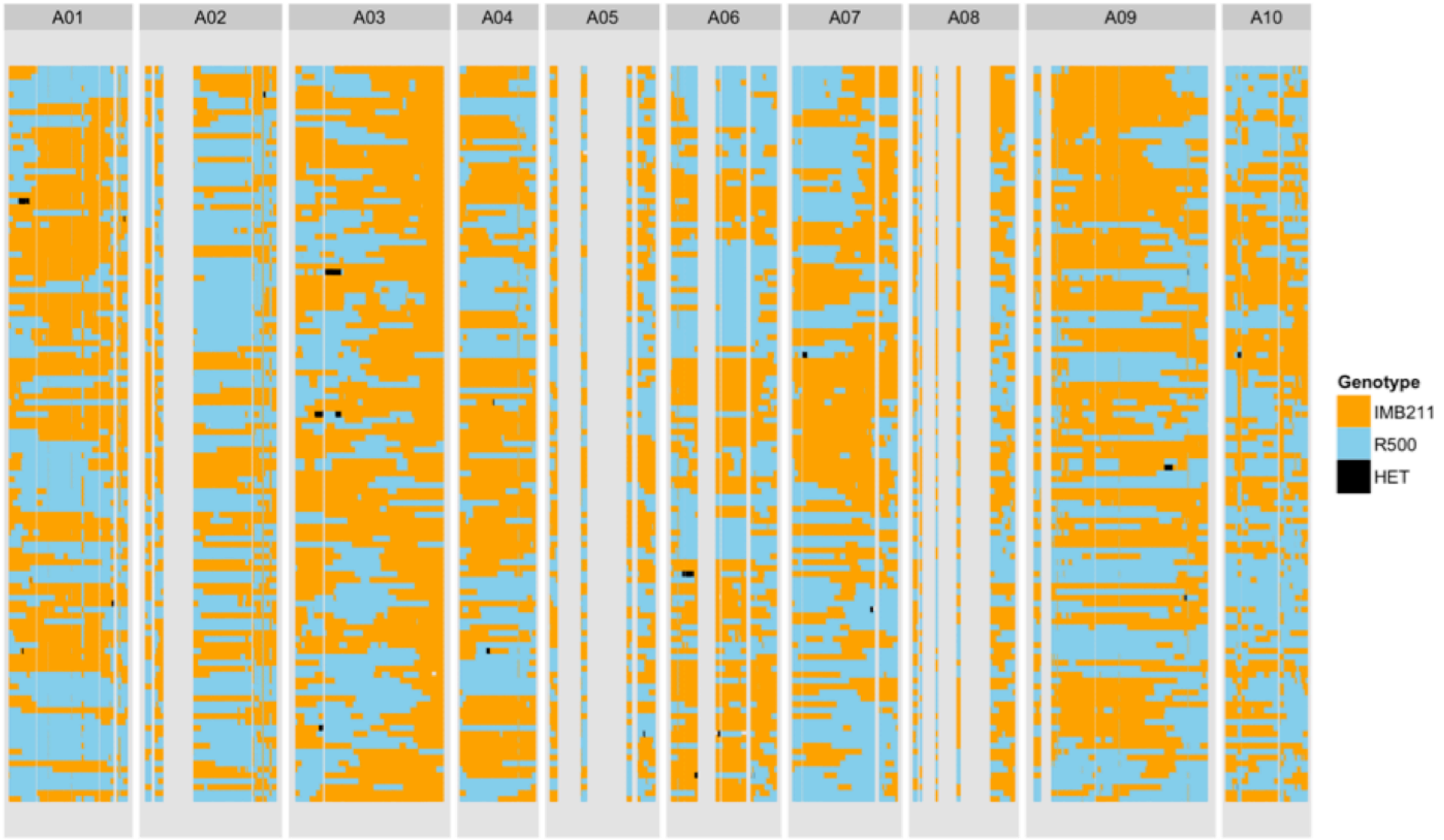
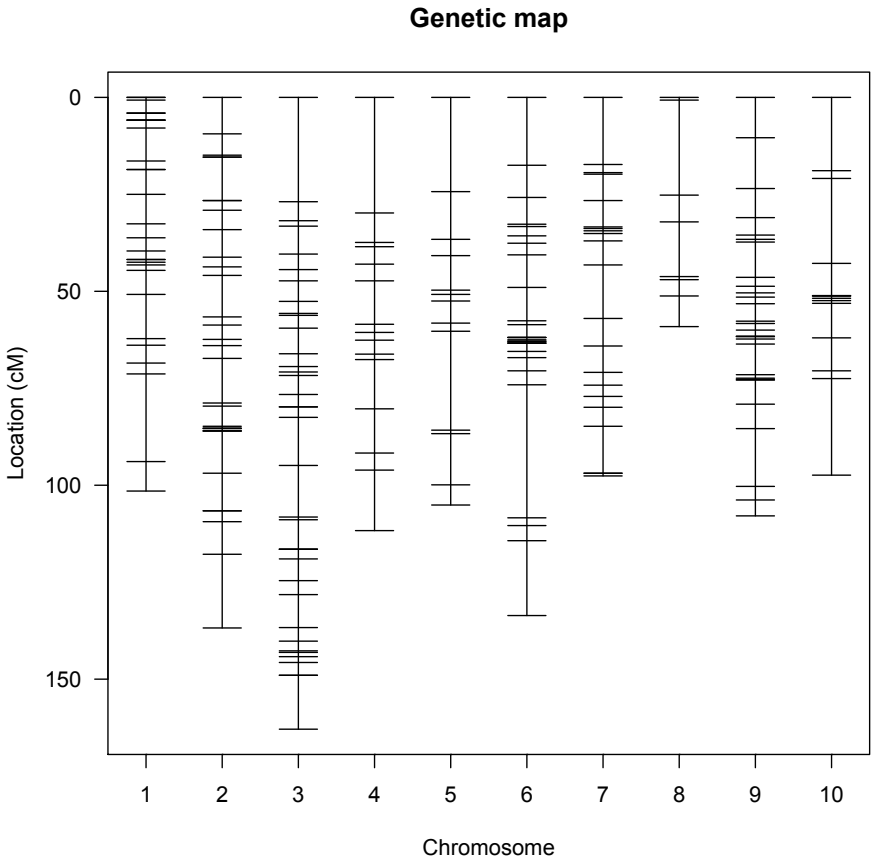
Genome Scale Sequencing Data

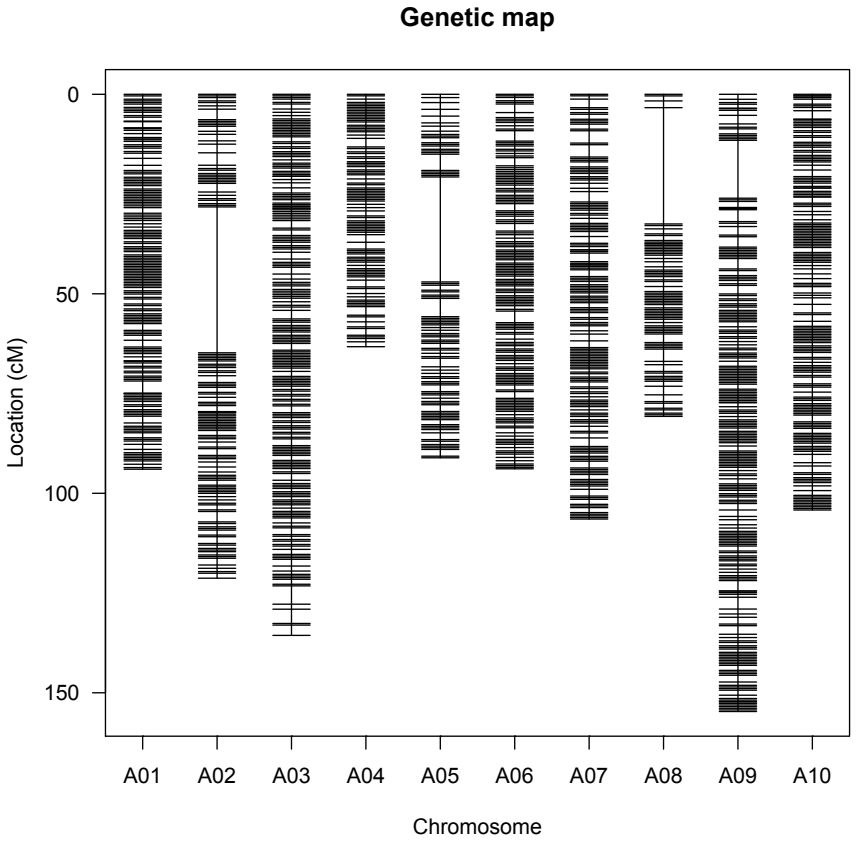


True mosaic of the parental genotypes

Improved Genetic Map

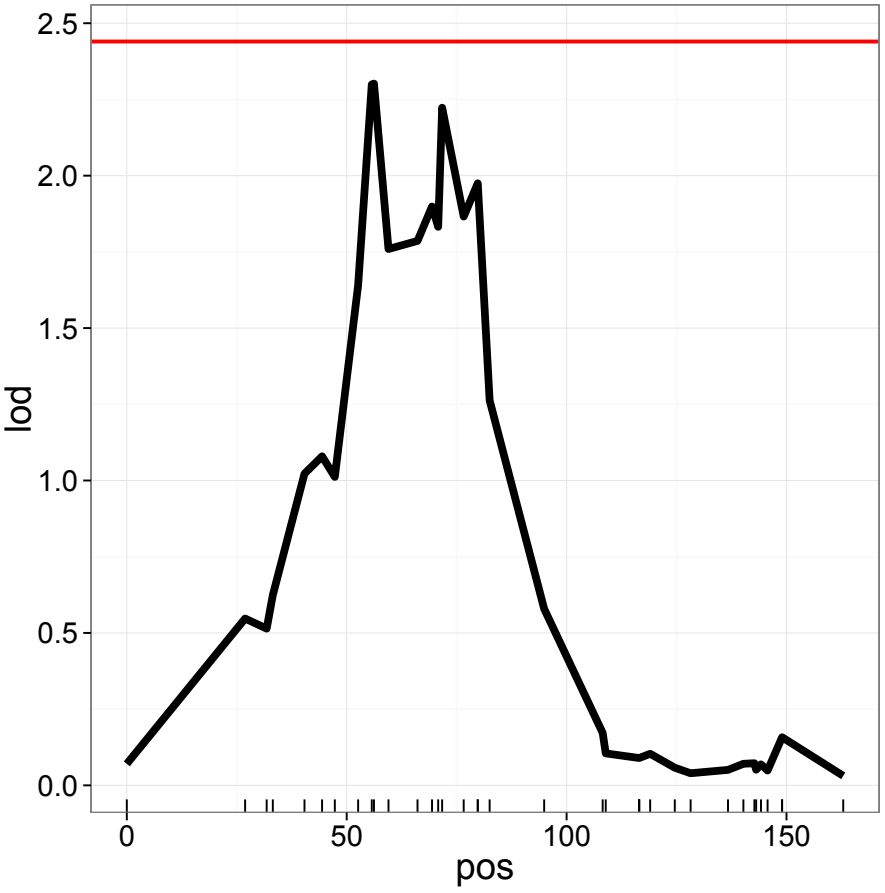


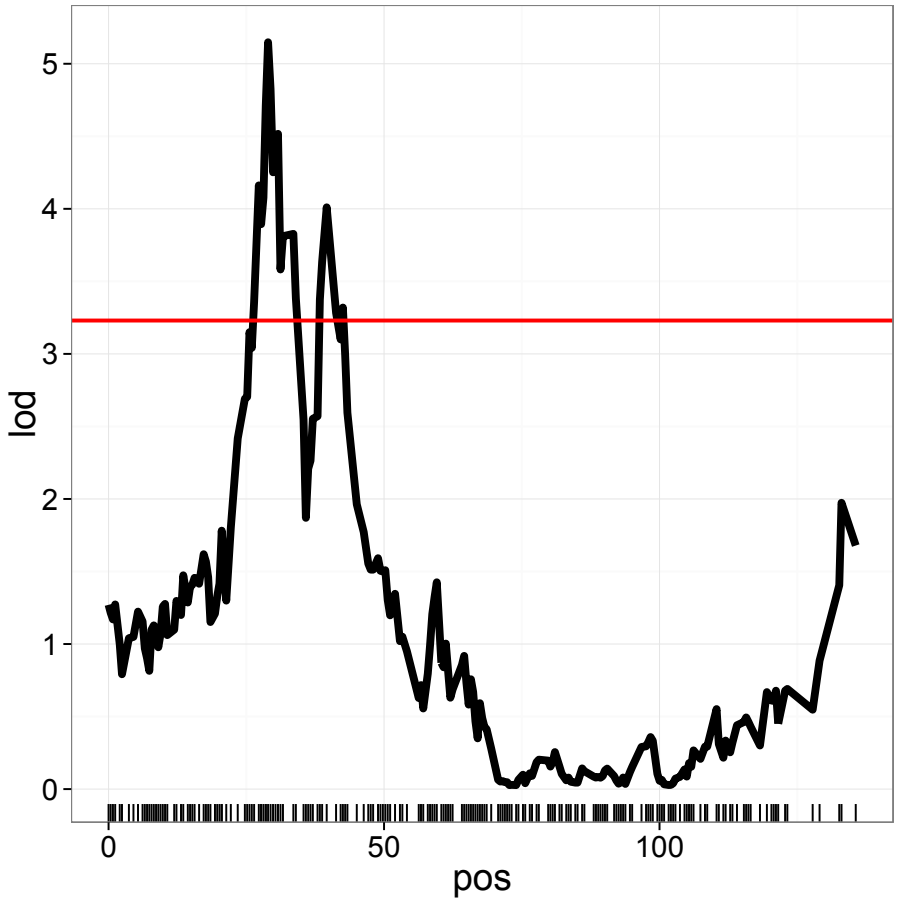
225 Markers
Difficult to anchor to genomic location



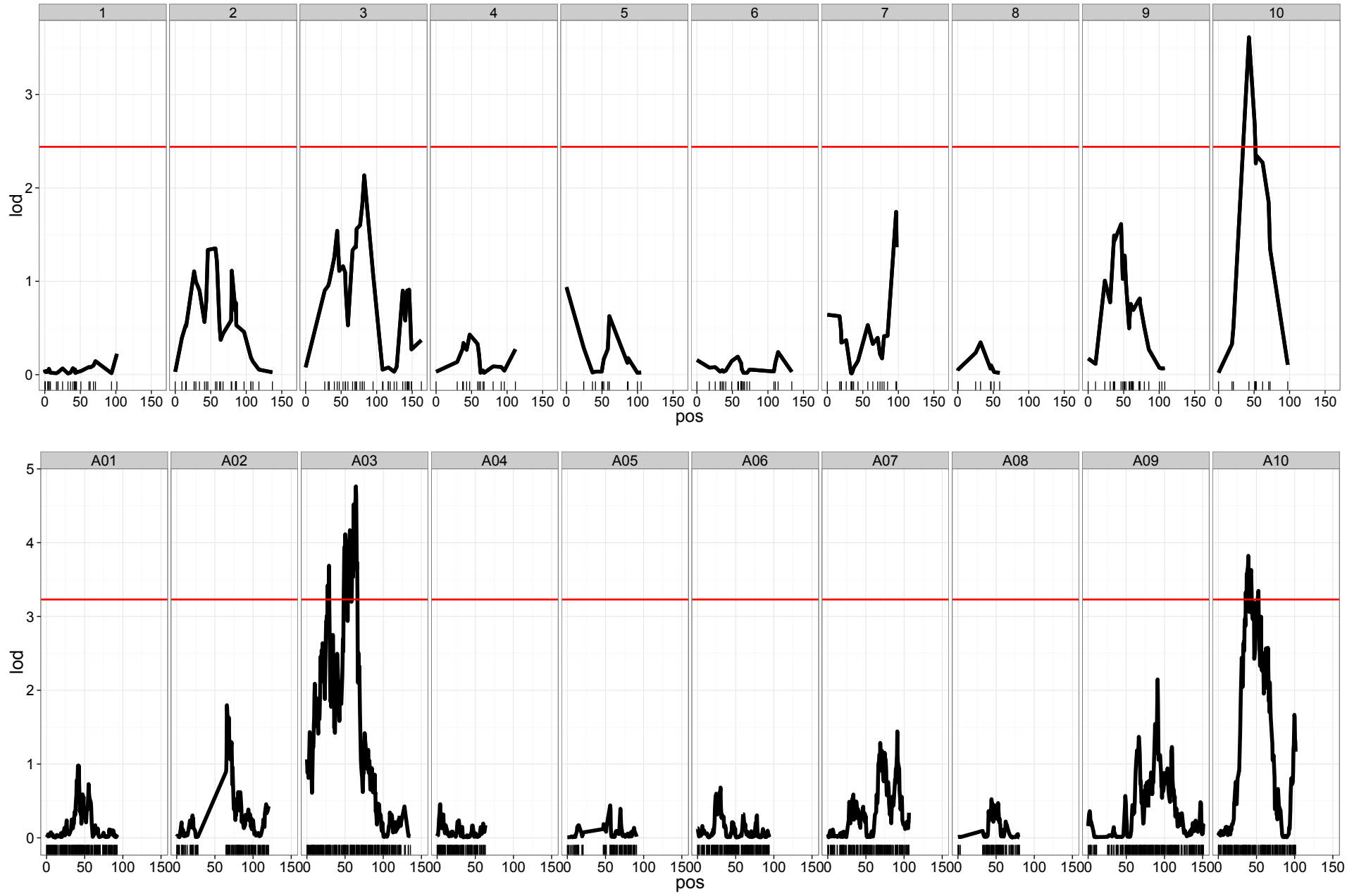
1400+ markers with known genomic coordinates

Plant Height





New map improves mapping resolution for known QTL



Remap all known traits in the population using new genetic map

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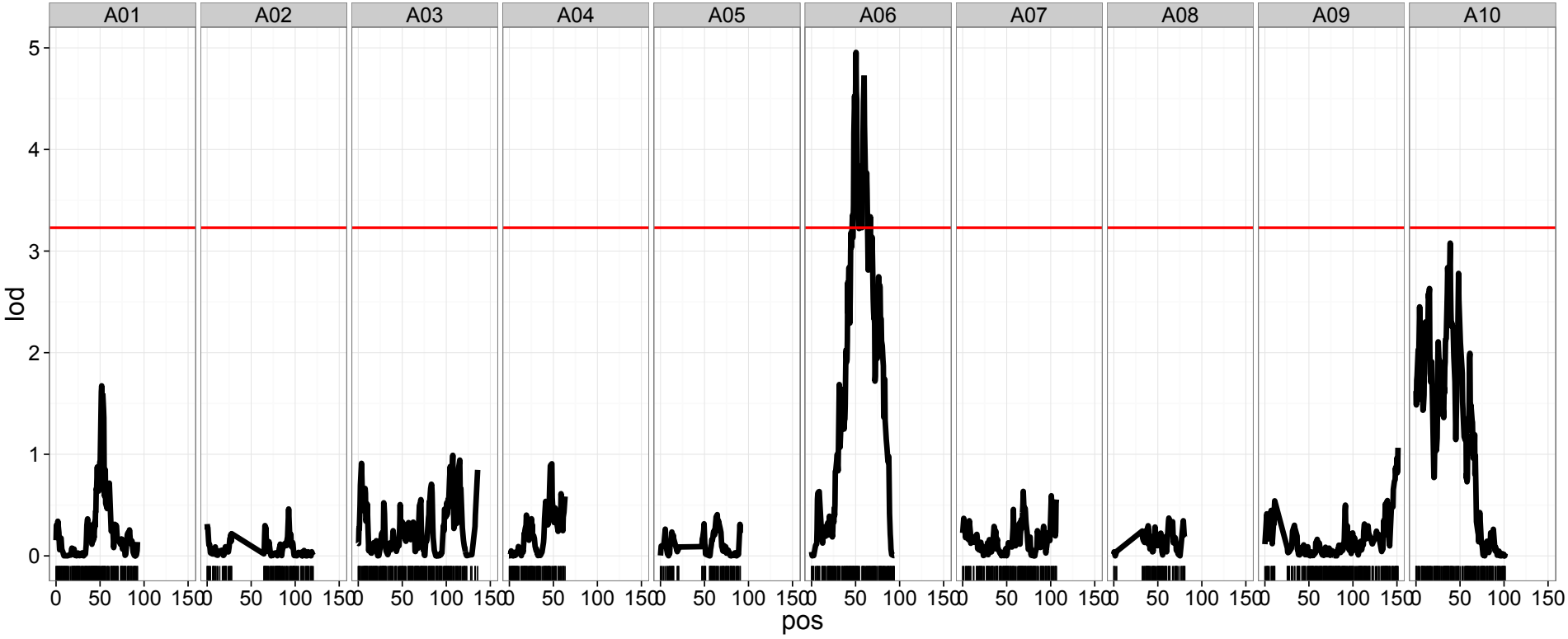
Gene Expression QTL (eQTL)

Polymorphism → Differential Gene Expression

- Can we find causative genes underlying physiological QTL by identifying *cis*-eQTL?

Cis and Trans eQTL example



Gene is located on chromosome A10, but peak for its expression also on A06

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Thanks!

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Postdoctoral Research Fellowships in Biology