R/qtl2

high-dimensional data and multi-parent populations

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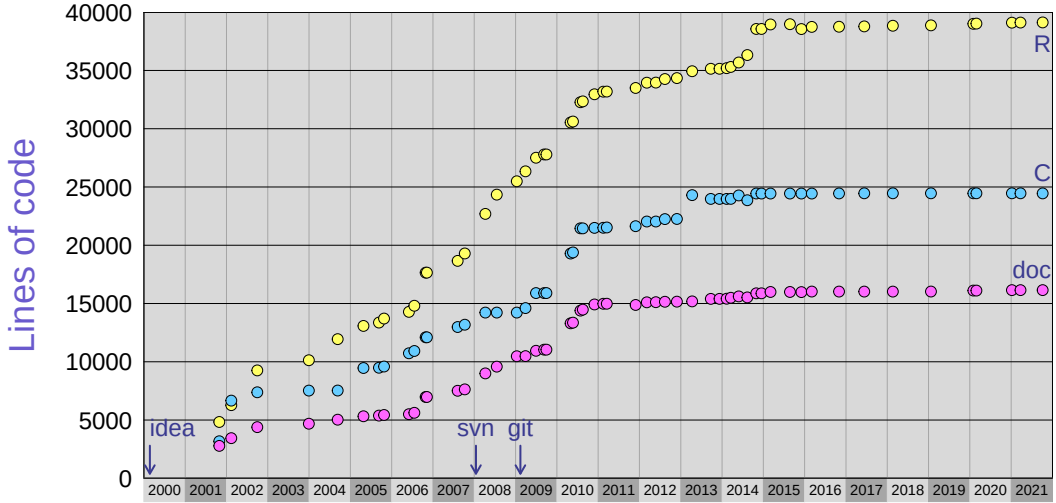
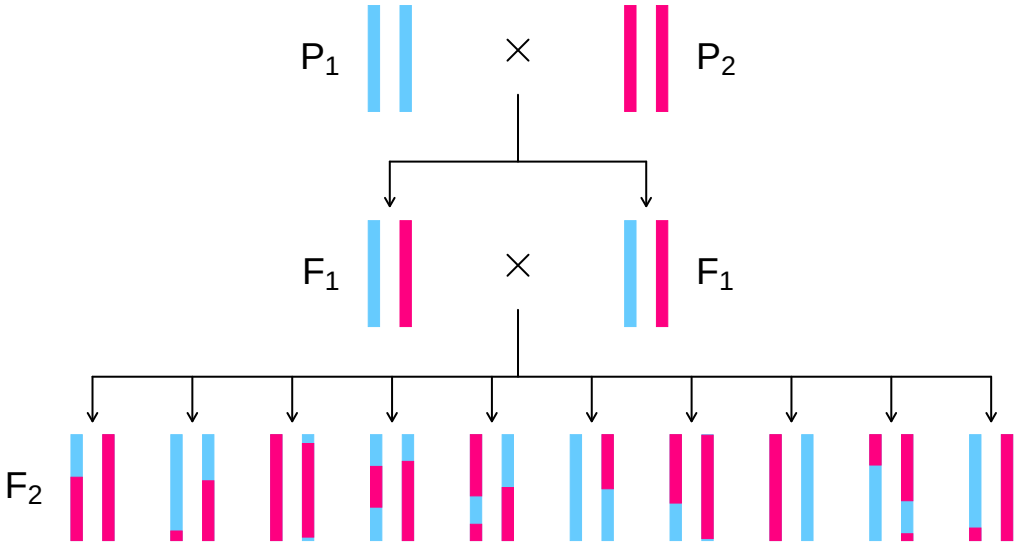
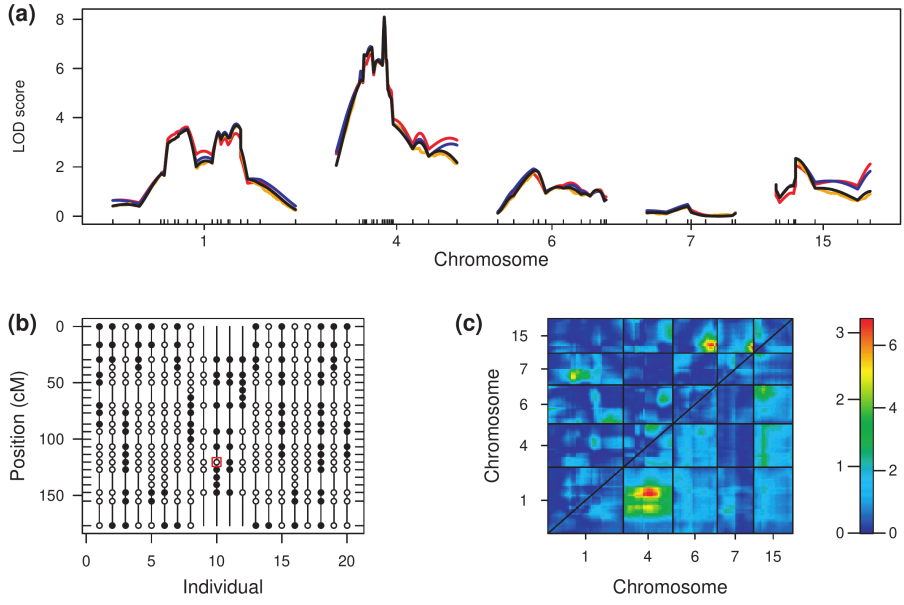
Slides: kbroman.org/Talk_DOWorkshop2021

21 years of R/qtl



Intercross





Broman et al. (2003) doi.org/bsjrwj

Good things

- efficient handling of missing genotypes
- diagnostics and data visualization
- fit and exploration of multiple-QTL models
- quite comprehensive
- quite flexible

Why work on software?

- to be useful
- makes our own analyses easier
- platform for implementing new methods
- has led to many collaborations

Bad things

- some really bloated code
- hard to maintain
- many inconsistencies in the user interface
- largely restricted to two-parent crosses

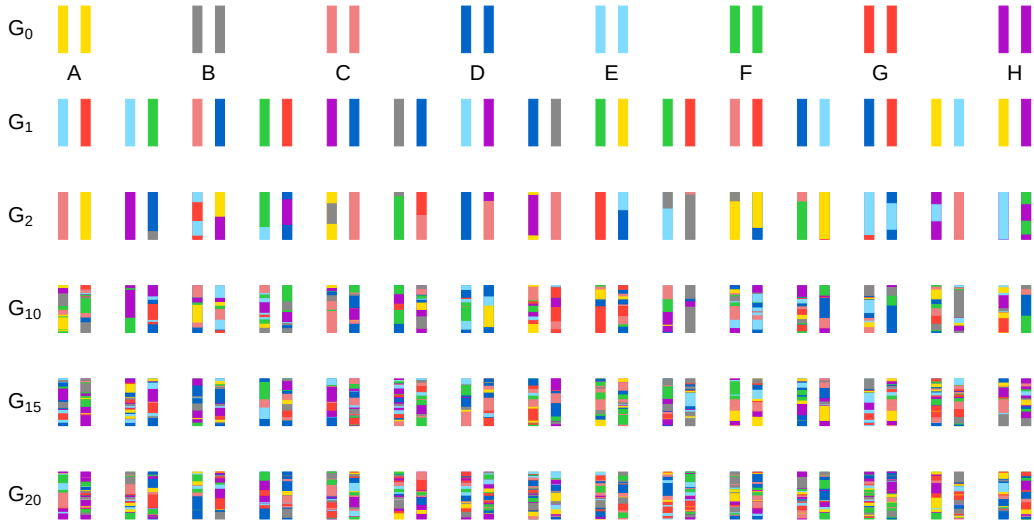
What's changed in 20 years?

- Genome sequence
- Larger crosses
- Denser SNP genotypes
- Gene expression and other omics data
- Multi-parent populations (MPPs)
- But still hard to find genes underneath QTL

Improving precision

- more recombinations
- more individuals
- more precise phenotype
- lower-level phenotypes
  - transcripts, proteins, metabolites

HS/DO




R/qt12
How in 3D

R/qtl2

- High-density genotypes
- High-dimensional phenotypes
- Multi-parent populations
- Linear mixed models

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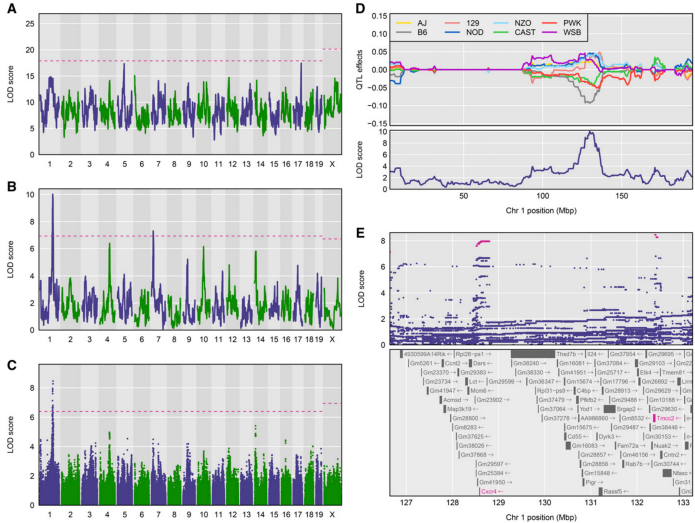
QTL mapping in MPPs

- Data diagnostics/cleaning
- Genome reconstruction
- QTL analysis
- Visualization/exploration of results

Genome reconstruction

QTL mapping in MPPs



Broman et al. (2019) doi.org/gfvknr

R/qtl2 plans

- Handling of GBS-based genotypes
- QTL$\times$QTL and QTL$\times$covariate interactions
- Multiple causal SNPs within a region

GWAS vs linkage

- Study design?
  - Natural population vs experimental cross
- Organism?
  - Human vs mouse
- Analysis method?
  - SNP alleles vs founder haplotypes

Fine-mapping a QTL

- Is there a SNP that accounts for the effect?
- Or some set of SNPs?
- Nature of genes; nature of SNPs within genes?
- Gene expression pattern that matches QTL effect?
- Gene expression that mediates the QTL effect?
- External information: QTL in human or rat?

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