

QTL mapping in MAGIC populations

Part 1

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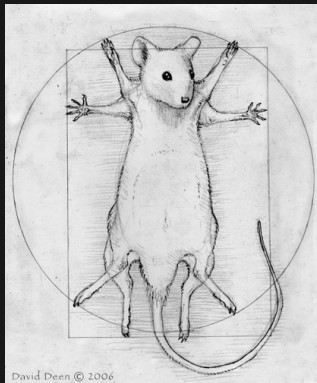
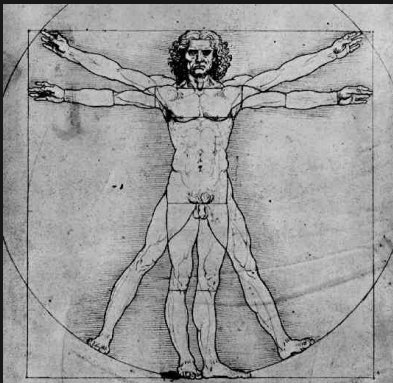
github.com/kbroman

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Slides: kbroman.org/Talk_MAGIC2021

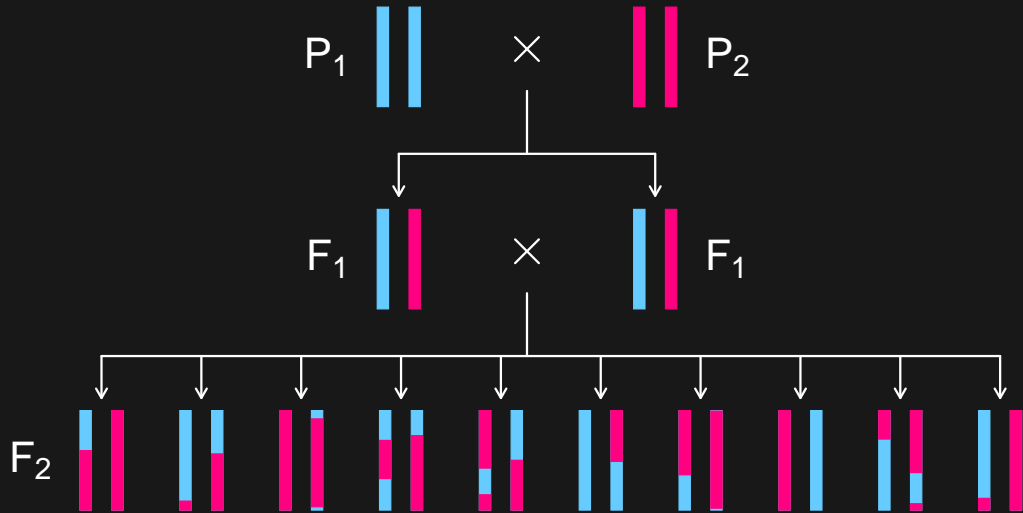




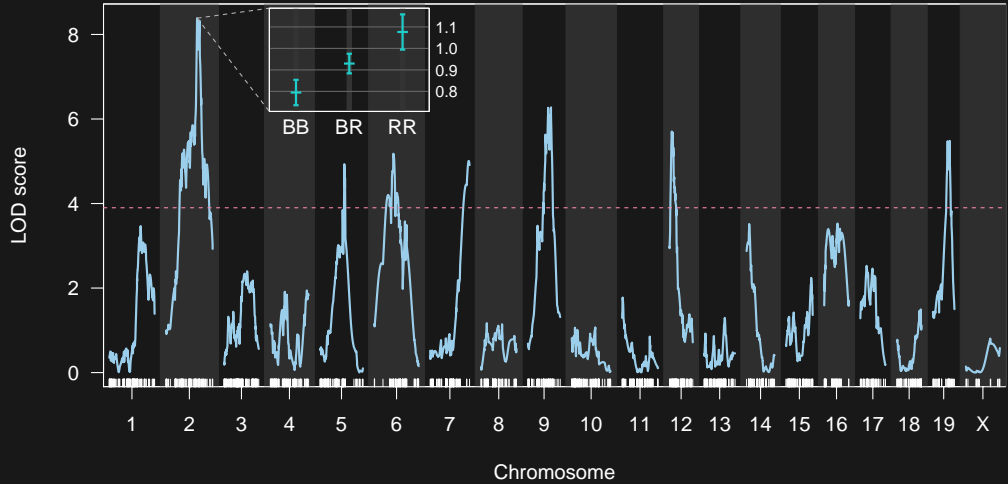


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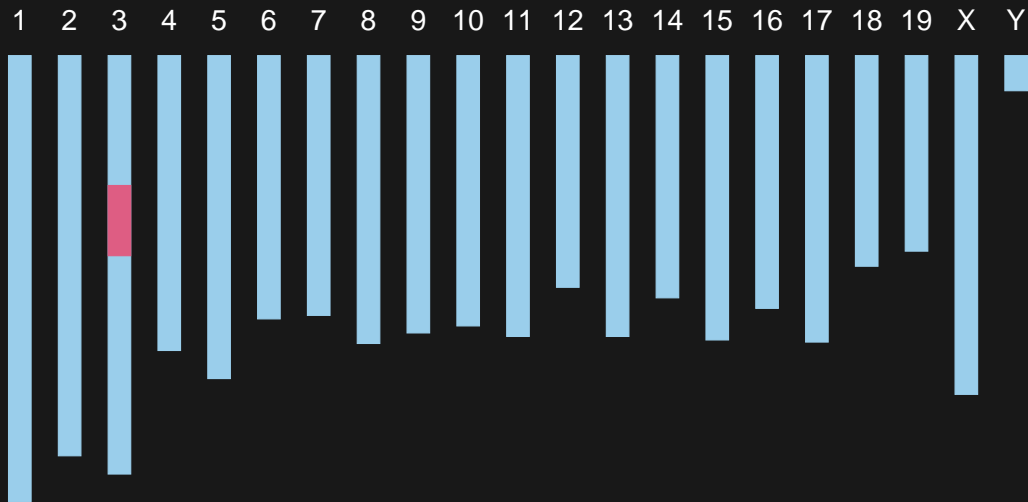
Intercross



QTL mapping



Congenic line/NIL



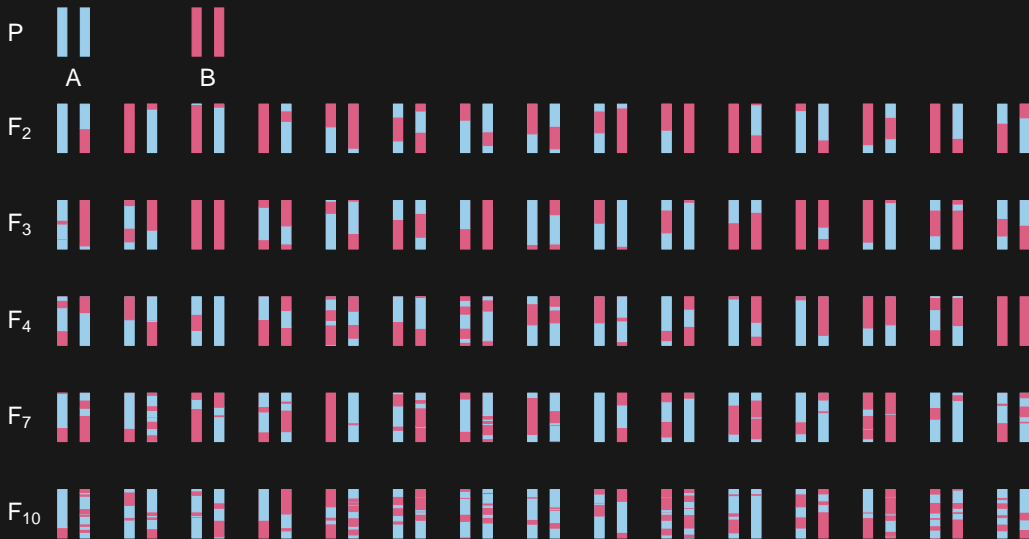
Improving precision

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

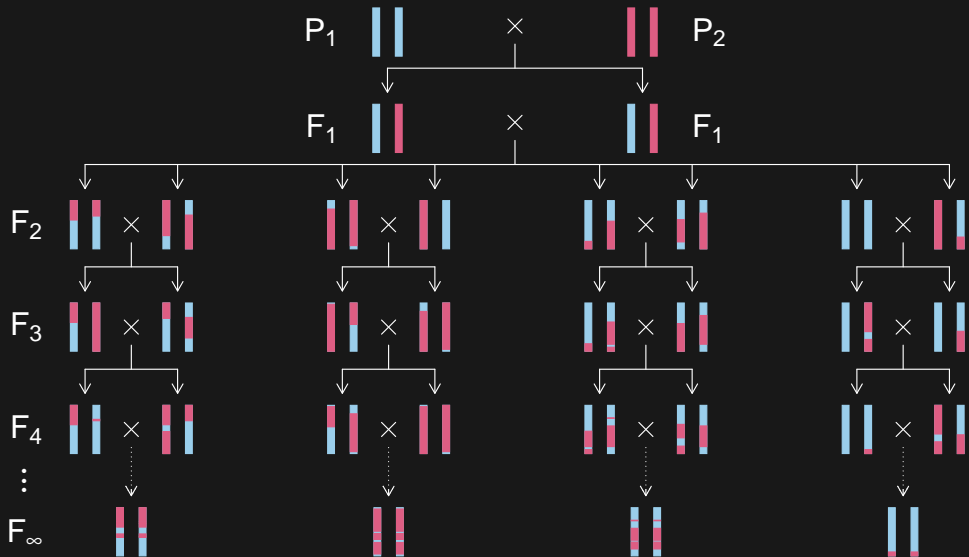
Genome-scale phenotypes



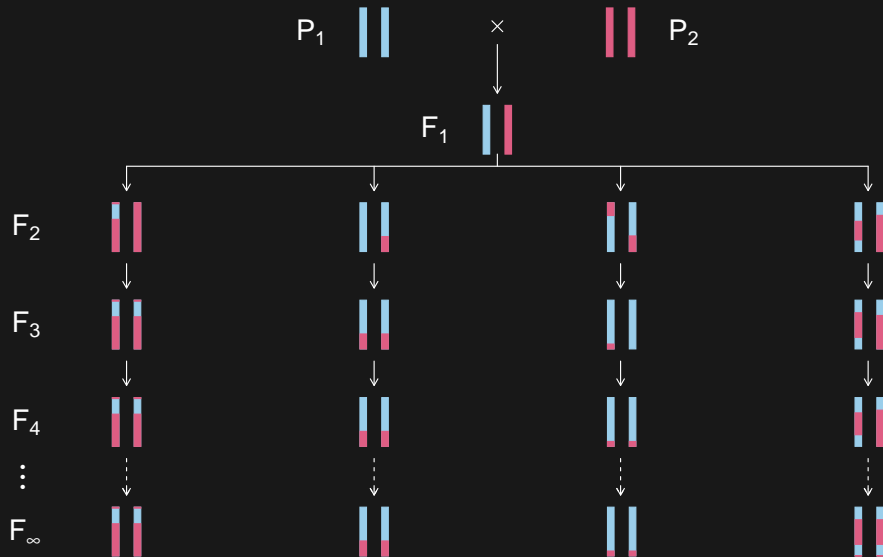
Advanced intercross lines



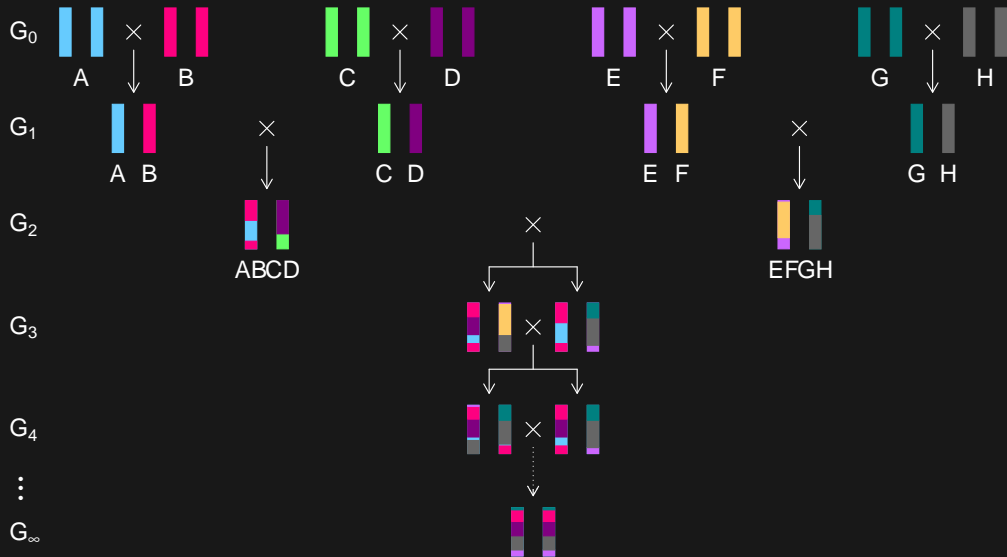
Recombinant inbred lines



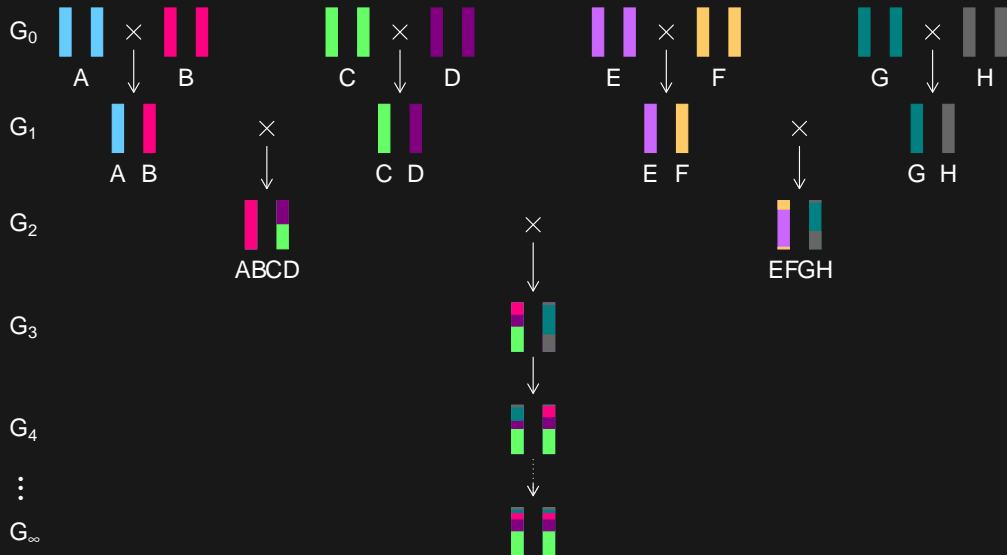
Recombinant inbred lines



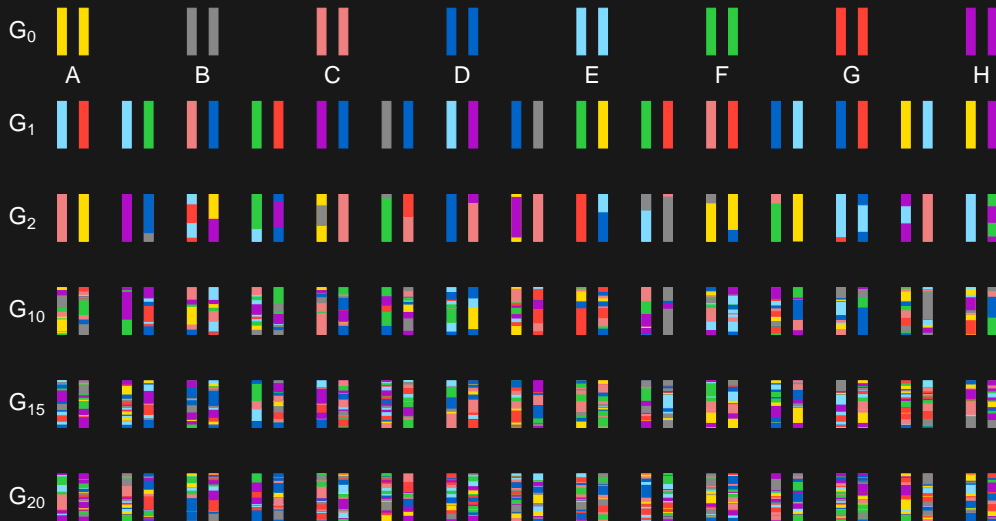
Collaborative Cross



MAGIC



Heterogeneous stock



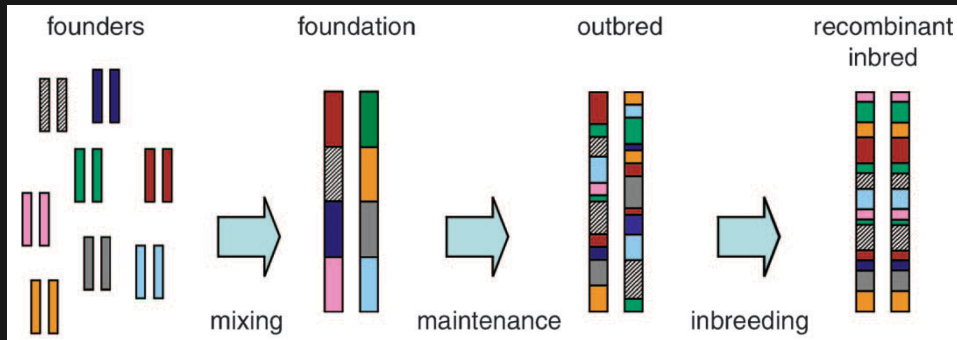
MAGIC is magic

- ▶ Genetic diversity
- ▶ High-precision mapping
- ▶ Predictable linkage disequilibrium
- ▶ Phenotype replicates to reduce individual variation
- ▶ Pool phenotypes from multiple labs, environments, treatments
- ▶ Genotype once

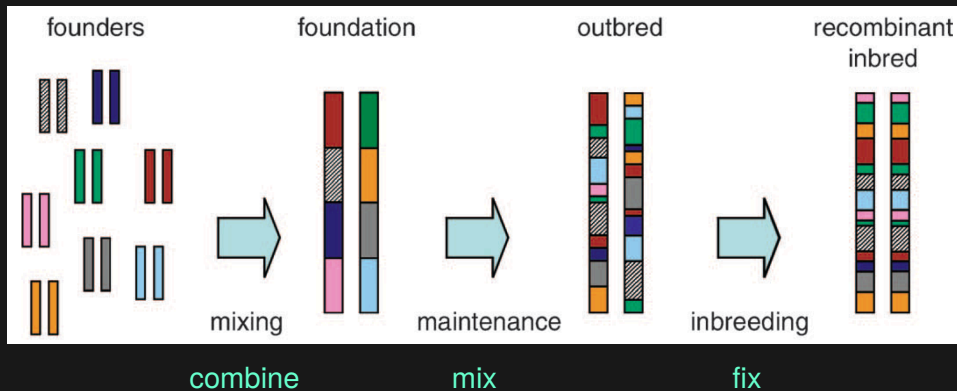
MAGIC is magic

- ▶ Genetic diversity
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- ▶ Genotype once
- ▶ Cool name

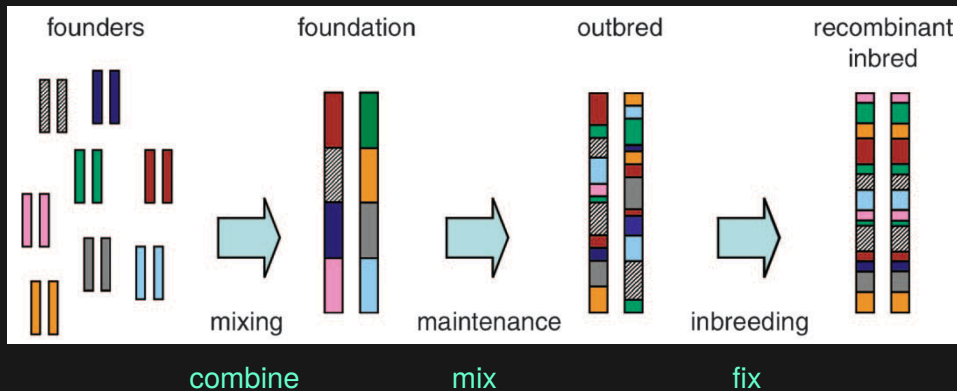
MAGIC lines



MAGIC lines

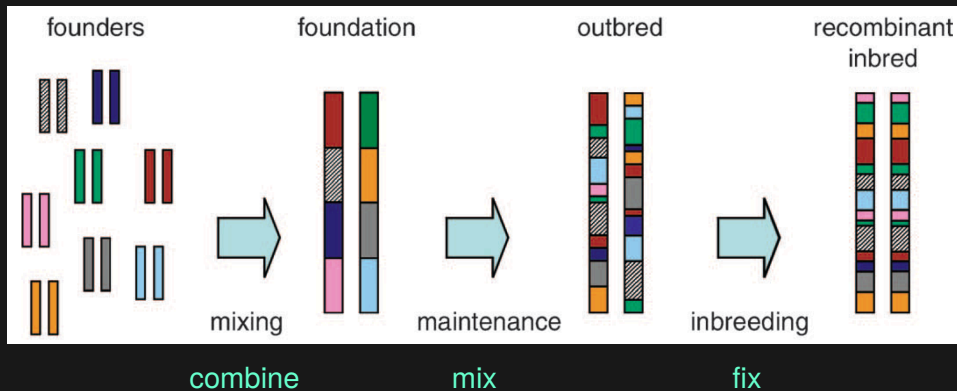


MAGIC lines



How many?

MAGIC lines

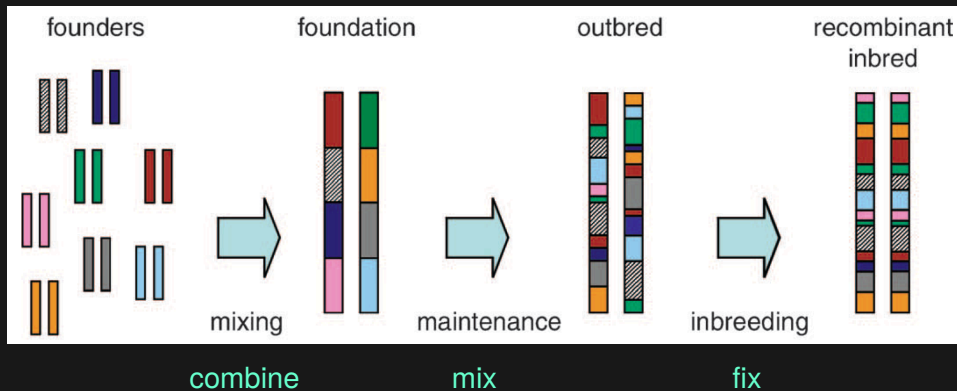


How many?

Which?

Valdar et al., Genetics 172:1783, 2006

MAGIC lines



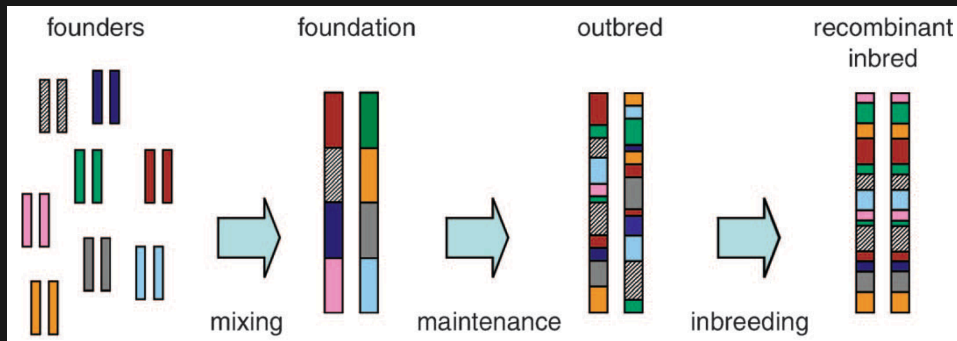
How many?

How long?

Which?

Valdar et al., Genetics 172:1783, 2006

MAGIC lines



combine

mix

fix

How many?

How long?

How?

Which?

Valdar et al., Genetics 172:1783, 2006

The goal

Identify QTL

- ▶ Power
- ▶ Mapping precision

The goal

Identify QTG

- ▶ Power
- ▶ Mapping precision

The goal

Identify QT**G**

- ▶ Power
- ▶ Mapping precision
- ▶ Estimate QTL allele frequencies

Principles

- ▶ Avoid population structure
- ▶ Tradeoff between *power for de novo discovery* and *mapping precision*
- ▶ More QTL to find \Rightarrow more QTL getting in the way?
- ▶ More QTL alleles \Rightarrow less information about each
- ▶ Are QTL alleles common or rare?

How many founders?

More

- ▶ More general use
- ▶ More QTL
- ▶ Greater precision
- ▶ Estimate allele frequencies
- ▶ Haplotype analysis in founders

Fewer

- ▶ Lower residual variance
- ▶ Greater power for a particular QTL?
- ▶ Better power for epistasis
- ▶ Rare alleles are less rare

Which founders?

- ▶ Diverse
- ▶ Interesting
- ▶ No breeding problems
- ▶ Balanced: star phylogeny

How much mixing?

- ▶ More mixing \Rightarrow Greater mapping precision
- ▶ ...but lower power for *de novo* mapping
- ▶ Potential for population structure, missing alleles
- ▶ Random mating or curated mating?
- ▶ Start with many random cross directions?

Selfing or DH?

- ▶ Inbreeding gives added recombination
- ▶ But not so much as at the mixing stage
- ▶ If doubled haploids are feasible, use them

Sharing is also key

- ▶ The greatest power of MAGIC comes from sharing
Pooling data, exploring multiple environments/treatments
- ▶ Common software needs
Analysis software, database infrastructure
- ▶ Many students need to learn the same stuff
Joint training opportunities

Summary

- ▶ How many founders?
 - Tradeoff between **diversity** and information about **particular alleles**
- ▶ Which founders?
 - Diverse, interesting, no breeding problems, star phylogeny
- ▶ How long to mix?
 - Tradeoff between **power** and **precision**
- ▶ How to fix?
 - Doubled haploids are great if feasible
- ▶ Let's share!
 - Lines, data, software, training

Slides: kbroman.org/Talk_MAGIC2021



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