QTL mapping in MAGIC populations Part 1

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daviddeen.com

Intercross



QTL mapping



Congenic line/NIL



Improving precision

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

Genome-scale phenotypes



Alan Attie

Advanced intercross lines



Recombinant inbred lines



Recombinant inbred lines



Collaborative Cross



MAGIC

 G_4

:

G∞





Heterogeneous stock



MAGIC is magic

- Genetic diversity
- ► High-precision mapping
- Predictable linkage disequilibrium
- ► No rare alleles
- Phenotype replicates to reduce individual variation
- ► Pool phenotypes from multiple labs, environments, treatments
- ► Genotype once

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- ► Cool name



Valdar et al., Genetics 172:1783, 2006



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The goal

Identify QTL



Mapping precision

The goal

Identify QTG



Mapping precision

The goal

Identify QTG



- 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?
- \blacktriangleright 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?

- \blacktriangleright 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



► 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

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