What is Quantitative Genetics?
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The theory of the statistical relationship between genotypic variation and phenotypic variation.
Quantitative Genetics

• Genotype
  The genetic constitution of an organism or cell; also refers to the specific set of alleles inherited at a locus

• Phenotype
  Any measurable characteristic of an individual, such as height, arm length, test score, hair color, disease status, migration of proteins or DNA in a gel, etc.

Looking for covariation between markers and phenotypes
Genetic Architecture: “sum” of the genetic effects upon a phenotype, including additive, dominance and parent-of-origin effects of several genes, pleiotropy and epistasis.
What Can You Do With Quantitative Genetics?
What Can You Do With Quantitative Genetics?

What is the genetic and environmental contribution to the phenotype?
How many genes influence the trait?
What are the genes and alleles controlling my trait?
Are these phenotypes controlled by the same genes?
Are the contributions of the genes equal?
How do alleles at different loci interact: additively? epistatically?
How rapid will the trait change under selection?
What are the genes causing a disease?
What lines should be crossed in my breeding program?
Key Concepts

• Quantitative variation
• Genetic by Environment Interactions
• Heritability
• Recombination
• QTL mapping
• GWAS
Discrete Traits

Discontinuous characteristic

Number of individuals

Phenotype (height)

Tall

Dwarf
Quantitative Traits

Continuous characteristic

Number of individuals

Dwarf  Tall
Phenotype (height)

Figure 24.1b
Genetics: A Conceptual Approach, Fifth Edition
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Alleles and Quantitative Traits

Number of individuals

Dwarf

AA

Aa

aa

Tall

Figure 24.2
Genetics: A Conceptual Approach, Fifth Edition
© 2014 W. H. Freeman and Company
Quantitative Traits are the Result of Genetics, Environment, and the interaction of Genetics and the Environment

Phenotype = Genotype + Environment + Genotype x Environment

Nature vs Nurture
Nature and Nurture
Traits can be Influenced by the Environments

Clausen, Keck, and Hiesey

The paper discusses the work of Clausen, Keck, and Hiesey on a long-term project titled Experimental Studies on the Nature of Species (ESNOS), which studied variation in plant populations in California. One of their best-known studies was on clinal variation in the yarrow, Achillea. They examined this species along a transect that ran from the Pacific coast well up into the Sierra Nevada range, observing a characteristic pattern of variation in the different environments, with taller plants in the San Joaquin valley and shorter plants at high altitude.
Traits are Influenced by Genotype x Environment Interactions
Quantitative Traits are the Result of Genetics, Environment, and the interaction of Genes and the Environment

Phenotype = Genotype + Environment + Genotype x Environment

$$V_P = V_G + V_E + V_{GE}$$
• Phenotype (P) = Population Mean ($\mu$) + Genotype (G) + Environment (E)

• Partition the variance of these components
  • Phenotypic variance = genetic variance + unexplained variance
    • This partitioning can only be performed at the level of a population

• Broad-sense heritability
  • $H^2 = \frac{\text{Var}(G)}{\text{Var}(P)}$

• Broad-sense heritability includes additive, dominance, epistatic variance, and parent-of-origin effects
Heritability

• Genetic (G) = Additive (A) + Dominance (D) + Imprinted (I) + Epistasis (E)

• \( \text{Var}(G) = \text{Var}(A) + \text{Var}(D) + \text{Var}(I) + \text{Var}(E) \)

• Narrow-sense heritability
  • \( h^2 = \frac{\text{Var}(A)}{\text{Var}(P)} \)

• Narrow-sense heritability is the ratio of the additive genetic variance to the total phenotypic variance
Heritability

- Ranges from 0 (all environmental) to 1 (all genetic)

- Specific to a population in specific environmental circumstances

- Highly inbred population with no genetic variation
  - Heritability of 0

- No environmental variance in an outbred population if all genetic variance is additive
  - Heritability of 1

- Most traits have a heritability between 0.2 and 0.8

- Can decrease by either a decrease in additive variance ($V_A$) or by an increase in environmental variance ($V_E$)
Measuring Heritability

(a) Heritability $\approx 0$

Midoffspring height (average height of offspring)

Tall

Short

Midparent height (average height of mother and father)

Short Tall
Measuring Heritability

(b) Heritability $\approx 0.5$

Midparent height (average height of mother and father)

Midoffspring height (average height of offspring)
Measuring Heritability

Midparent height (average height of mother and father)

(c) Heritability ≈ 1

Midoffspring height (average height of offspring)

Tall

Short

Tall

Short
In total, 4892 NAM and IBM RILs were scored for height in 7 environments.

This resource contains 2815 inbreds from worldwide maize gene pools. Inbreds were planted in single-row plots and evaluated for PHT, EHT, and DTA in three environments: Aurora, NY; Clayton, NC; & Columbia, MO.
Trait Heritability

• What are 4 highly heritable traits?
• What are 4 traits with low heritability?
• How would you set up an experiment to test this?
Linkage Disequilibrium

**Not Linked**
Gene 1 and Gene 2 are far apart on the same chromosome.

**Linked**
Gene 3 and Gene 4 are close together on the same chromosome.

Non-random association of alleles at different loci

Slide from Lawson
## Linkage Disequilibrium (LD)

<table>
<thead>
<tr>
<th>Haplotype</th>
<th>Frequency</th>
<th>Allele</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>$A_1B_1$</td>
<td>$X_{11}$</td>
<td>$A_1$</td>
<td>$p_1 = X_{11} + X_{12}$</td>
</tr>
<tr>
<td>$A_1B_2$</td>
<td>$X_{12}$</td>
<td>$A_2$</td>
<td>$p_2 = X_{21} + X_{22}$</td>
</tr>
<tr>
<td>$A_2B_1$</td>
<td>$X_{21}$</td>
<td>$B_1$</td>
<td>$q_1 = X_{11} + X_{21}$</td>
</tr>
<tr>
<td>$A_2B_2$</td>
<td>$X_{22}$</td>
<td>$B_2$</td>
<td>$q_2 = X_{12} + X_{22}$</td>
</tr>
</tbody>
</table>

$$D = X_{11} - p_1q_1$$

Correlation coefficient $r = \frac{D}{\sqrt{p_1 \cdot p_2 \cdot q_1 \cdot q_2}}$

Slide from Lawson
Decay of Linkage Disequilibrium
Human Chromosome 22

Slide from Lawson
Recombination is not uniform

cM = Genetic distance: 1% chance of crossover

Genome-wide recombination rate variation in a recombination map of cotton- Plos One 2017

https://doi.org/10.1371/journal.pone.0188682
Key Concepts

- Quantitative variation
- Genetic by Environment Interactions
- Heritability
- Recombination
- QTL mapping
- GWAS

Looking for covariation between markers and phenotypes
Genetic Mapping

So many flavors
Genetic Mapping

- Constructed or Assembled
- What parents
- What markers
- What environments are you working in
- What phenotyping are you using
- What statistical approach

So many flavors
Start with an F2
Recombinant Inbred Line

Marker loci = M + numbers
Genotype  L = Ler
          C = Col

X Crossed
⊗ Self Crossed

F1

F2

F3

F8
Getting to homozygous lines

Doubled haploid wheat breeding - instant homozygous wheat lines

Parents

F1 Year 1

Haploid

100% homozygous doubled haploid

F2 Year 2

F3 Year 3

F4 Year 4

F5 Year 5

F6 Year 6

F7 Year 7

F8 Year 8

99.2% homozygous

Traditional Breeding Methods

Doubled Haploid Breeding

Coloradowheat.org
QTL Mapping

The maize intermated B73xMo17 (IBM) population
R/qtl: A QTL mapping environment

Software for mapping quantitative trait loci in experimental crosses

Current version: 1.66 (2023-11-27)

[ Download | FAQ | News | Bugs | Sample graphics | Sample data | Tutorials | Book | Manual | Citation ]

Try the R/qtlcharts package: interactive graphics for QTL data.


See the R/qtl source code on GitHub; licensed under GPL-3.
Variation among IBM recombinant inbred lines is described with 4,000 bi-allelic SNPs.
Variation among IBM recombinant inbred lines is described with 4,000 bi-allelic SNPs.
Quantitative trait locus (QTL) mapping isolates genetic regions influencing a trait.
LOD score

LOD Score = \log_{10}\left(\frac{\text{Probability of test statistic if linkage}}{\text{Probability of test statistic if random}}\right)

Other methods use \(-\log_{10}(p\text{-value})\)
Permutation to determine significance

Magnesium (ppm)

Frequency

Genotype data

Markers

Individuals

1  2  3  4  5  6  7  8  9  10

1000 2000 3000 4000
Quantitative trait locus (QTL) mapping isolates genetic regions influencing a trait

Stepwise forward / backward regression
The Interaction of Genotype and Environment Determines Variation in the Maize Kernel Ionome

Alexandra Asaro,* Gregory Ziegler,† Cathrine Ziyomo,* and Ivan Baxter†,1

| Table 1 Broad-sense heritability (H²) of element concentrations |
|------------------|--------|--------|--------|--------|
| Trait            | All Env | NY05   | NC06   | MO06   |
| Seed weight      | 0.30    | 0.59   | 0.69   | 0.89   |
| B                | 0.02    | 0.35   | 0.51   | 0.06   |
| Na               | 0.07    | 0.34   | 0.23   | 0.19   |
| Mg               | 0.04    | 0.77   | 0.69   | 0.75   |
| Al               | 0.07    | 0.39   | 0.50   | 0.08   |
| P                | 0.03    | 0.62   | 0.69   | 0.33   |
| S                | 0.05    | 0.73   | 0.77   | 0.51   |
| K                | 0.06    | 0.69   | 0.72   | 0.36   |
| Ca               | 0.12    | 0.65   | 0.63   | 0.77   |
| Mn               | 0.14    | 0.80   | 0.80   | 0.75   |
| Fe               | 0.07    | 0.76   | 0.73   | 0.63   |
| Co               | 0.06    | 0.65   | 0.54   | 0.42   |
| Ni               | 0.05    | 0.84   | 0.54   | 0.82   |
| Cu               | 0.17    | 0.80   | 0.75   | 0.92   |
| Zn               | 0.07    | 0.68   | 0.73   | 0.86   |
| As               | 0.02    | 0.37   | 0.45   | 0.01   |
| Se               | 0.03    | 0.32   | 0.35   | 0.68   |
| Rb               | 0.03    | 0.49   | 0.45   | 0.69   |
| Sr               | 0.06    | 0.61   | 0.48   | 0.53   |
| Mo               | 0.23    | 0.85   | 0.73   | 0.96   |
| Cd               | 0.36    | 0.71   | 0.69   | 0.24   |

1. Role of research associate in genetics and agronomy is not specified.
The Interactions Between Ionomes and Molybdenum QTLs

Alexandra Asaro,* C and Ivan Baxter†,1

A. Molybdenum QTL

B. Ionome QTL Mapped in 10 environments

C. Cd, Mo, Sr, Rb, Se, As, Zn, Cu, Ni, Co, Cd, Fe, Mn, Ca, K, S, P, Al, Mg, Na, Weight

D. Nickel QTL

[Graphs and tables showing genetic interactions and data analysis]
How many genes under the peak?
Fine Mapping

- Heterzygous Inbred Families (HIFs)
- Near isogenic lines (NILs)

Modified Quantitative Hybrid Complementation Test
QTL Mapping Summary

• Lots of statistical power
• Can replicate the experiment in multiple environments
• Creating populations requires the investment of time and resources
Bulk Segregant Analysis (BSA)

- Flips the paradigm: uses phenotypes to pool and sequence to determine allele composition.
- Can do in F2 populations.

![Diagram showing phenotypic classes and genetic loci](image)
Genome Wide Association Mapping

- Uses genetically diverse populations
- Many different alleles
- Uses the recombinations in the history of the population
Linkage and Association

Linkage

Association

20 Generations
Chromosome Segregation
Chromosome Segregation
Chromosome Segregation