# Day 2
# Quantitative Genetics: Additive Effects

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# AlphaSimR Implementation

- Select loci to serve as causal loci (QTL)
- Sample initial additive QTL effects
  - Usually from a standard normal distribution
- Scale magnitude of effects to achieve a desired variance ($V_A = V_G$)
- Add a constant to achieve a desired mean

| Genotype | 0 | 1 | 2 |
|---|---|---|---|
| Genetic Value | -a | 0 | a |

# Understanding Variance Scaling

- What is the variance of the additive effects?
  - Additive variance is a fixed variable
  - Treating allele frequencies as fixed variables (for simplicity)
  - Additive effects are random variables

- Starting with simplifying assumptions
  - AlphaSimR doesn’t depend on these assumptions

- Assumptions
  - Population in Hardy-Weinberg Equilibrium (HWE)
  - No linkage disequilibrium (LD) between loci
  - Only additive effects (i.e. average effect = additive effect)

# Additive Variance with HWE and no LD

$$V_A = 2\sum_{i=1}^{nQTL} p_i q_i \alpha_i^2$$

# Expectations for Random Variables

$$\alpha = a$$

$$a \sim N(0, \sigma_a^2)$$

$$E(\alpha^2) = E(a^2) = \sigma_a^2$$

# Rewrite to Show Trends

$$E(\sigma_a^2) = \frac{V_A}{2\sum_{i=1}^{nQTL} p_i q_i}$$

$$E(\sigma_a^2) \propto V_A$$

$$E(\sigma_a^2) \propto y$$

$$y \approx \frac{1}{nQTL}$$

# Change the Assumptions

- Remove the HWE assumption
  - $2pq\alpha^2$ becomes $2(1+F)pq\alpha^2$
    - $2pq$ and $2(1+F)pq$ represent variance of genotype dosage
  - Effects become smaller for a given variance when F>0
  - Conversely, inbreeding increases variance when effects are fixed
    - When there are only additive effects

- Consider LD
  - Measure of covariance between loci at gamete level
    - D = prob(AB) – prob(A)*prob(B)
  - Simulations usually start with LD in initial population
  - Doesn’t really change anything (see next slide)

# Additive Variance with HWE and LD

$$V_A = 2\sum_{i=1}^{n} p_i q_i \alpha_i^2 + 4\sum_{i=1}^{n-1}\sum_{j=i+1}^{n} D_{i,j}\alpha_i \alpha_j$$

$$E(\alpha_i \alpha_j) = 0$$

# Does LD Matter?

- Yes, it matters a lot
  - Just not when applying additive effects to our initial population
- Our initial population is unselected
  - With respect to the additive effects being assigned
- The important properties of LD occur under selection
  - Bulmer effect

# Bulmer Effect

- Selection induces LD
  - Truncation or stabilizing selection creates negative LD
    - Lowers genetic variance
  - Disruptive selection creates positive LD
    - Increases genetic variance
- Induced LD dissipates during mating
  - Depends on recombination rate
- Effect also applies to multiple traits
  - Changes genetic correlation between traits

# Bulmer's Partitioning of Variance

- Bulmer partitions genetic variance into three components
  - Genic variance
    - Expected variance with HWE and no LD
  - Covariance due to departure from HWE
  - Covariance due to linkage

- Total genetic variance is the sum of these components

# AlphaSimR Demonstration