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AlphaSimR Implementation

- Select loci to serve as causal loci (QTL)
- Sample initial additive QTL effects

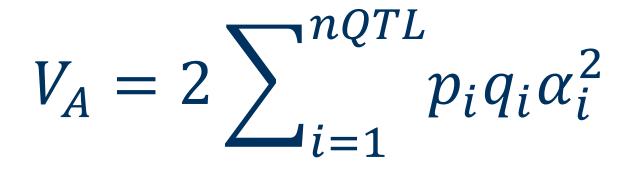
 Usually from a standard normal distribution
- Scale magnitude of effects to achieve a desired variance $(V_A = V_G)$
- Add a constant to achieve a desired mean

Genotype	0	1	2
Genetic Value	-a	0	а

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



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