EQGW 2025
Lecture 1: Intro to Quant Gen

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Lecture One Objectives

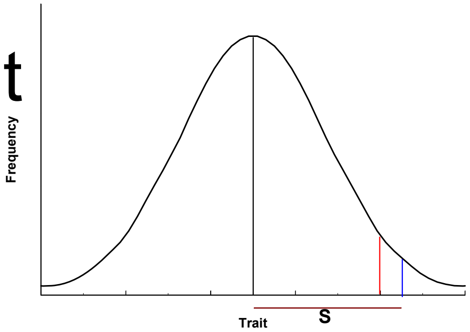
1) Define components of phenotypic variance in terms of allelic frequencies, allelic values & environment.

2) Define resemblances among relatives in terms of components of phenotypic variances.

3) Consider selection and evolution from a quantitative genetic perspective.

Basic Quant Gen:

- Assumes each of many (infinite) loci contribute (infinitesimally) small amounts to a continuous phenotypic trait
- If family relationships in the population are known, the phenotype can be partitioned into Genetic and Environmental components:



$P_i = G_i + E_i$

Furthermore, G can be partitioned

$G = A + D + I$

D = dominance effects = interactions among alleles within a locus

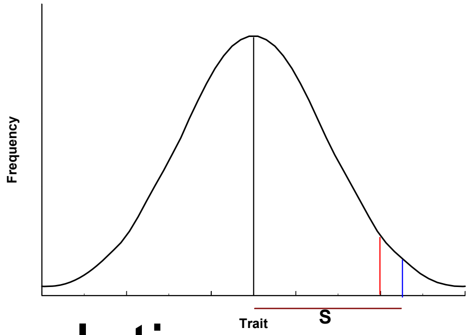
I = Epistatic effects = interactions among loci

Breeding or Additive Genetic Value

- A = Breeding value = Additive Genetic Value = The value of an individual judged by the mean value of its progeny.
- If an individual is mated to a number of individuals taken at random from the population, then its breeding value is twice the mean deviation of its progeny from the population mean.
- This represents the portion of G passed from parents to offspring; i.e., the effect of allelic substitutions.
  - Note: D and I are interactions and cannot be passed directly from parent to offspring

Phenotypic Variance

- If family relationships in the population are known, the VARIANCE in the phenotype can also be partitioned:



$P_i = G_i + E_i$ where P_i is deviation from population mean

$V_P = \sum P_i^2/N$

$V_P = (G_i + E_i)^2/N$

$V_P = V_G + V_E + 2\text{cov}GE^*$

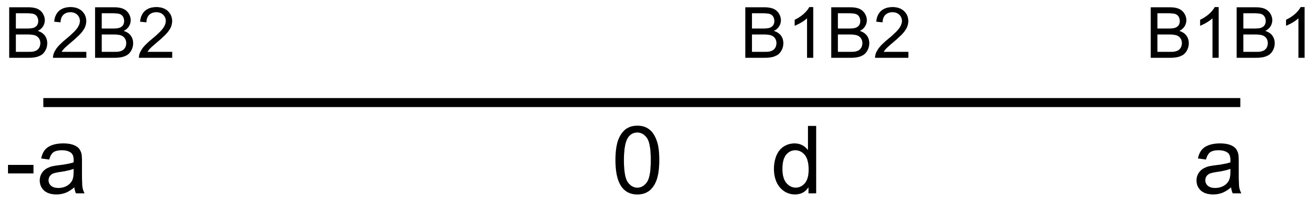
$V_G = V_A + V_D + V_I$

Heritability: $h^2 = V_A/V_P$

*(covGE is non-random association of genotype and environment-worry about this later)

Another Definition of V_A

- $V_A = 2pq[a+d(q-p)]^2$



B2B2 B1B2 B1B1

- -a 0 d a
- -a = phenotypic value of B2B2 genotype
- a = phenotypic value of B1B1 genotype
- 0 = mid-homozygous point
- d = dominance deviation (can be 0)
- V_A derived as deviation from pop mean
- Sum across all loci that contribute to Ptype

Another Definition of V_A

- $V_A = 2pq[a+d(q-p)]^2$
- p = frequency of B1 allele (a la H-W)
- q = frequency of B2 allele
- Sum across all loci that contribute to Ptype
- Additive effects depend on allelic values, as noted in previous slide
- Also depend on allele frequencies which means V_A is **population specific**!

Ways to Think about Variances

- **Phenotypic variance can be partitioned into "*causal* components" (V_A, V_D, etc.)**
- **Phenotypic variance can also be partitioned into components corresponding to grouping of individuals into families**
- **These are called "*observational* components" of variance, denoted by σ^2 (instead of V) and can be directly estimated and used to estimate *causal* components of variance.**

Ways to Think about Variances

$V_P = \sigma_B^2 + \sigma_w^2$ where

σ_B^2 = *between* family group variance around true pop mean
σ_w^2 = *within* family group variance around true family group mean

The greater the similarity within groups, the greater the difference between groups

Degree of resemblance can therefore be expressed as

$\frac{\sigma_B^2}{\sigma_B^2 + \sigma_w^2}$ which is called t, the intraclass correlation coefficient

σ_B^2 = amount of variation that is common to members of the same group, and so it is a type of <u>covariance</u>.

Ways to Estimate Family Covariances

- **Covariance among related individuals is a *population* property we want to estimate to find cause of resemblance among relatives**
- **Observational covariance is composed of causal components of variance, so we can use the observational covariance to estimate the causal components**
- **most common and useful family covariances are:**

  offspring and one parent
  offspring and two parents
  half sibs
  full sibs

Ways to Estimate Family Covariances: Objectives and Assumptions

- **Objective: deduce the covariances of relatives arising from genetic causes.**
- **Assume (initially) no contribution by non-genetic causes of resemblance**
- **Assume population in H-W equilibrium**
- **Assume random mating with regard to trait under consideration**
- **Assume (initially) no epistatic interactions**

Offspring and one parent

By definition, mean genotypic value of offspring is ½ the breeding value of the parent. Therefore, the covariance to be computed is that of an individual's genotypic value with half its breeding value:

Cov OP = Cov (½A)(G)   (recall that G = A + D)
= Cov (½A)(A + D)
= ½ Cov A^2 + ½ Cov AD
= ½ V_A + ½ Cov AD   (Cov AD = 0)
= ½ V_A

Offspring and mid-parent

$\mathrm{Cov}\ O\overline{P} = \mathrm{Cov}\ O([P_{♂} + P_{♀}]/2)$

$= (\mathrm{Cov}\ OP_{♂} + \mathrm{Cov}\ OP_{♀})/2$

$= (½\ V_{A♂} + ½\ V_{A♀})/2$

if $V_{A♂} = V_{A♀}$ then:

$= (½\ V_A + ½\ V_A)/2$

$= ½\ V_A$

Half-sibs (share one parent in common)

The mean genotypic value of half sibs is by definition half the breeding value of the common parent:

$$\text{Cov}_{hs} = \text{Cov}\,(\tfrac{1}{2}A)(\tfrac{1}{2}A) = \text{Cov}\,\tfrac{1}{4}A^2 = \tfrac{1}{4}V_A$$

Full-Sibs (share both parents in common)

Mean genotypic value of full sibs is equal to mean breeding value of the 2 parents:

$\mathrm{cov}_{FS} = \mathrm{cov}[\ \tfrac{1}{2}\ (A_{♂} + A_{♀})]^2$

$= \tfrac{1}{4}\ (V_{A♂} + V_{A♀})$

if $V_{A♂} = V_{A♀}$ then:

$= \tfrac{1}{4}\ (2V_A)$

$= \tfrac{1}{2}\ V_A + ?$

Because full sibs share both parents, they have the possibility of also sharing the parents' dominance deviation.

Full-Sibs: Dominance

- Let parents have genotypes A_1A_2 A_3A_4
- Offspring genotypes are A_1A_3 A_1A_4 A_2A_3 A_2A_4 each in 0.25 frequency
- Randomly choose any one sib (e.g., A_1A_4)
- The probability that the next sib chosen has the same genotype, and hence has the same dominance deviation is ¼
- On average then full sibs share dominance deviation ¼ of the time
- So: $\mathrm{cov}_{FS} = \frac{1}{2} V_A + \frac{1}{4} V_D$

General

- **The generalized covariance for any family relationship is**

  cov = $rV_A + uV_D$

  where r is the fraction of additive genetic variance and u is the fraction of dominance variance

- **Let P and Q be two individuals whose covariance is required, and A, B, C, and D be their respective parents, and f be the coancestry. Then**

  $r = 2f_{PQ}$
  $u = f_{AC}f_{BD} + f_{AD}f_{BC}$

- Note: f is the coancestry of 2 individuals and is:
  - Equivalent to inbreeding coefficient of their progeny if they were mated
  - Inbreeding coefficient = probability that offspring has 2 alleles identical by descent

Epistasis

Variance arising from epistatic interactions between loci contributes small fractions to the covariances of relatives. Hence the generalized covariance really is:

$$cov = rV_A + uV_D + r^2V_{AA} + ruV_{AD} + u^2V_{DD} + r^3V_{AAA} + etc$$

- **Only small fractions of the interaction components contribute to covariance (max is ¼)**
- **Interaction components involving dominance only contribute if dominance contributes**
- **Interactions of breeding values (e.g., V_{AAA}) contribute to all covariances**

Environmental Covariances

- **$V_E = V_{Ec} + V_{Ew}$**

  V_{Ec} is environment common to related individuals = nutrition, climate, culture, etc.

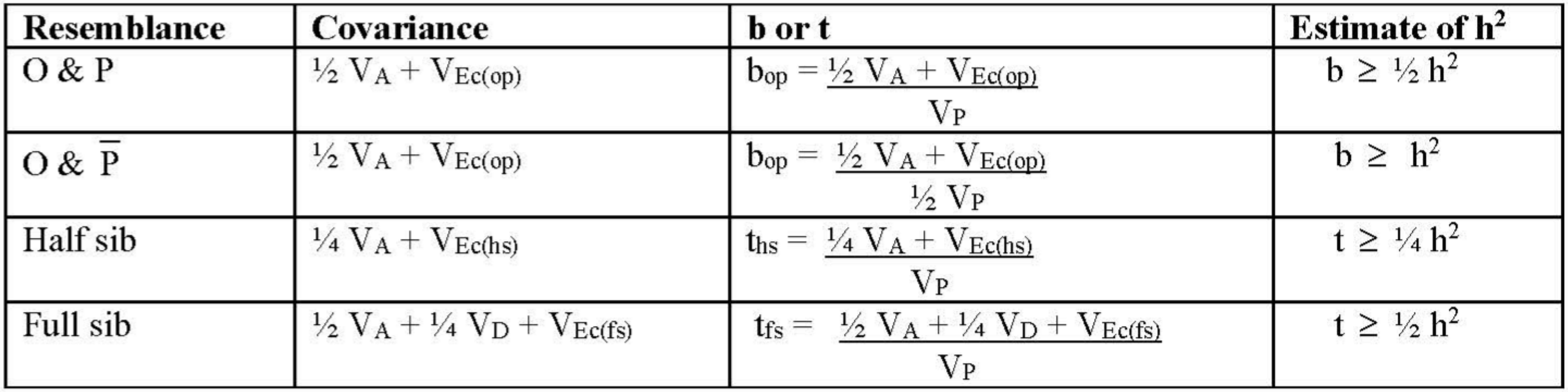
  try to eliminate with experimental design; e.g., randomize offspring over rearing environments

- **Maternal effects are a frequent source of V_{Ec}**

  example: large mice moms make more milk and so have larger pups = confounds parent-offspring estimates

  example: good mom mice have warm nests which affects tail length of pups (but not of moms) = confounds sib estimates

Phenotypic Resemblance



Resemblance	Covariance	b or t	Estimate of h^2
O & P	$\frac{1}{2} V_A + V_{Ec(op)}$	$b_{op} = \frac{\frac{1}{2} V_A + V_{Ec(op)}}{V_P}$	$b \geq \frac{1}{2} h^2$
O & $\overline{P}$	$\frac{1}{2} V_A + V_{Ec(op)}$	$b_{op} = \frac{\frac{1}{2} V_A + V_{Ec(op)}}{\frac{1}{2} V_P}$	$b \geq h^2$
Half sib	$\frac{1}{4} V_A + V_{Ec(hs)}$	$t_{hs} = \frac{\frac{1}{4} V_A + V_{Ec(hs)}}{V_P}$	$t \geq \frac{1}{4} h^2$
Full sib	$\frac{1}{2} V_A + \frac{1}{4} V_D + V_{Ec(fs)}$	$t_{fs} = \frac{\frac{1}{2} V_A + \frac{1}{4} V_D + V_{Ec(fs)}}{V_P}$	$t \geq \frac{1}{2} h^2$

Sib Study Classic ANOVA

Source	**df**	**Mean Square**	**Expected MS**
Between sires	s-1	MS_S	$\sigma^2_W + k\sigma^2_D + dk\sigma^2_S$
Between dams (sires)	s(d-1)	MS_D	$\sigma^2_W + k\sigma^2_D$
Within progenies	sd(k-1)	MS_W	σ^2_W

s = number of sires
d = number of dams per sire
k = number of offspring per dam

Observational Component	**Covariance**	**Causal Component**
Sires: $\sigma^2_S = (1/dk)(MS_S - MS_D)$	$\sigma^2_S = \text{cov}_{HS}$	$\frac{1}{4} V_A$
Dams: $\sigma^2_D = (1/k)(MS_D - MS_W)$	$\sigma^2_D = \text{cov}_{FS} - \text{cov}_{HS}$	$\frac{1}{4} V_A + \frac{1}{4} V_D + V_{Ec}$
Progeny: $\sigma^2_W = MS_W$	$\sigma^2_W = V_P - \text{cov}_{FS}$	$\frac{1}{2} V_A + \frac{3}{4} V_D + V_{Ew}$
Total	$\sigma^2_T = \sigma^2_W + \sigma^2_D + \sigma^2_S = V_P$	$V_A + V_D + V_{Ec} + V_{Ew}$
Sires + Dams	$\sigma^2_S + \sigma^2_D = \text{cov}_{FS}$	$\frac{1}{2} V_A + \frac{1}{4} V_D + V_{Ec}$

D. Phenotypic Resemblance

- **Why not use t for parents and offspring?**

$$t = \frac{\sigma_B^2}{\sigma_B^2 + \sigma_w^2} = \frac{\text{covariance among groups}}{\text{total variance}}$$

in sib studies, the total variance is easy to estimate; it is simply the variance of all the sibs.

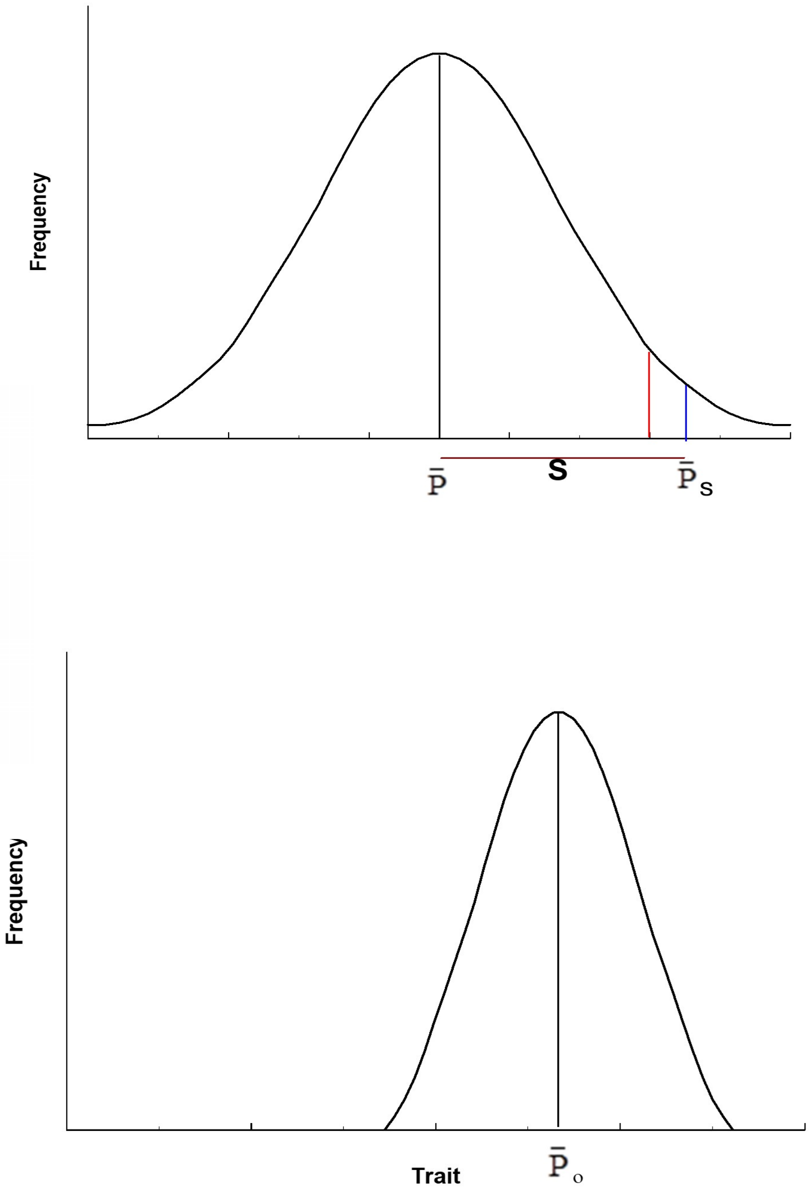
in parent offspring studies, the total variance basically must be estimated by the product of the standard deviation of the parents and the standard deviation of the offspring. This gets messy. However:

$$b_{y\ on\ x} = \frac{\text{cov(x)(y)}}{\text{variance of x}}$$

this is estimable in parent-offspring (but notice that it wouldn't work with sibs, because who is x and who is y)

$$b_{op} = \frac{\text{cov OP}}{\text{Var of parents}}$$

Selection



Population mean	$\bar{P}$
Mean of Selected Parents	$\bar{P}_s$
Offspring mean	$\bar{P}_o$
Selection differential	$S = \bar{P}_s - \bar{P}$
Response to selection	$R = \bar{P}_o - \bar{P}$

Selection

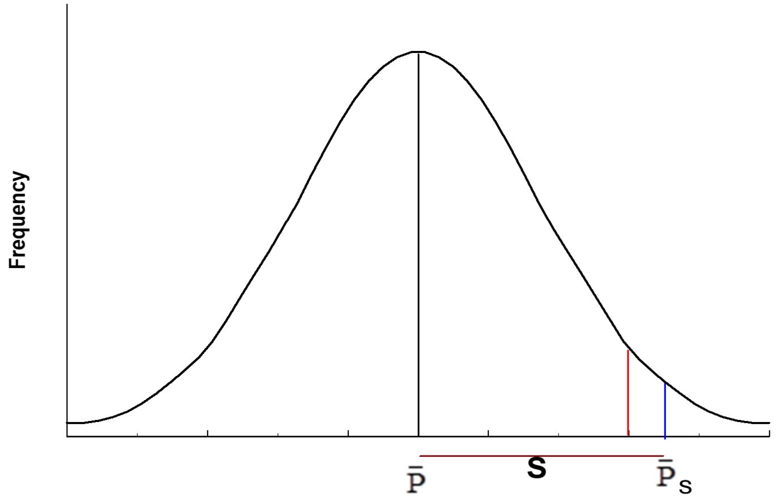
$$\hat{Y} = \overline{Y} + b_{yx}(x - \overline{x})$$

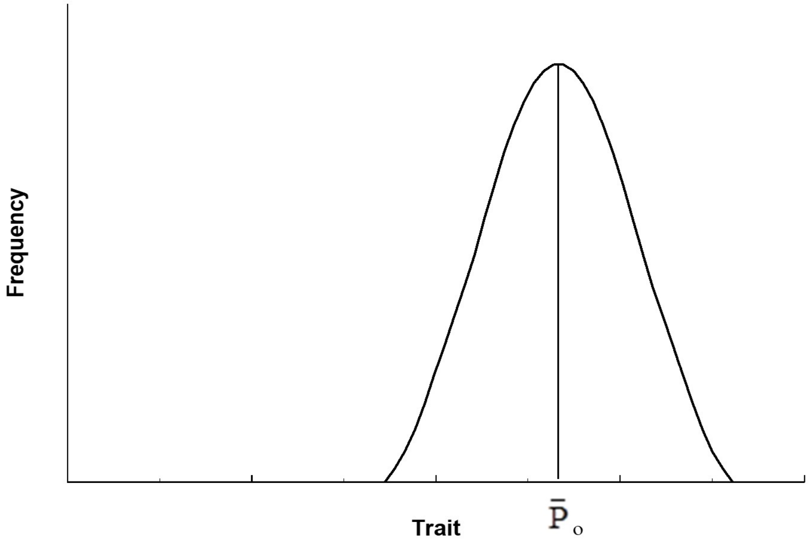
$$\overline{P}_o = \overline{P} + b_{o\overline{P}}(\overline{P}_s - \overline{P})$$

$$\overline{P}_o - \overline{P} = b_{o\overline{P}}(\overline{P}_s - \overline{P})$$

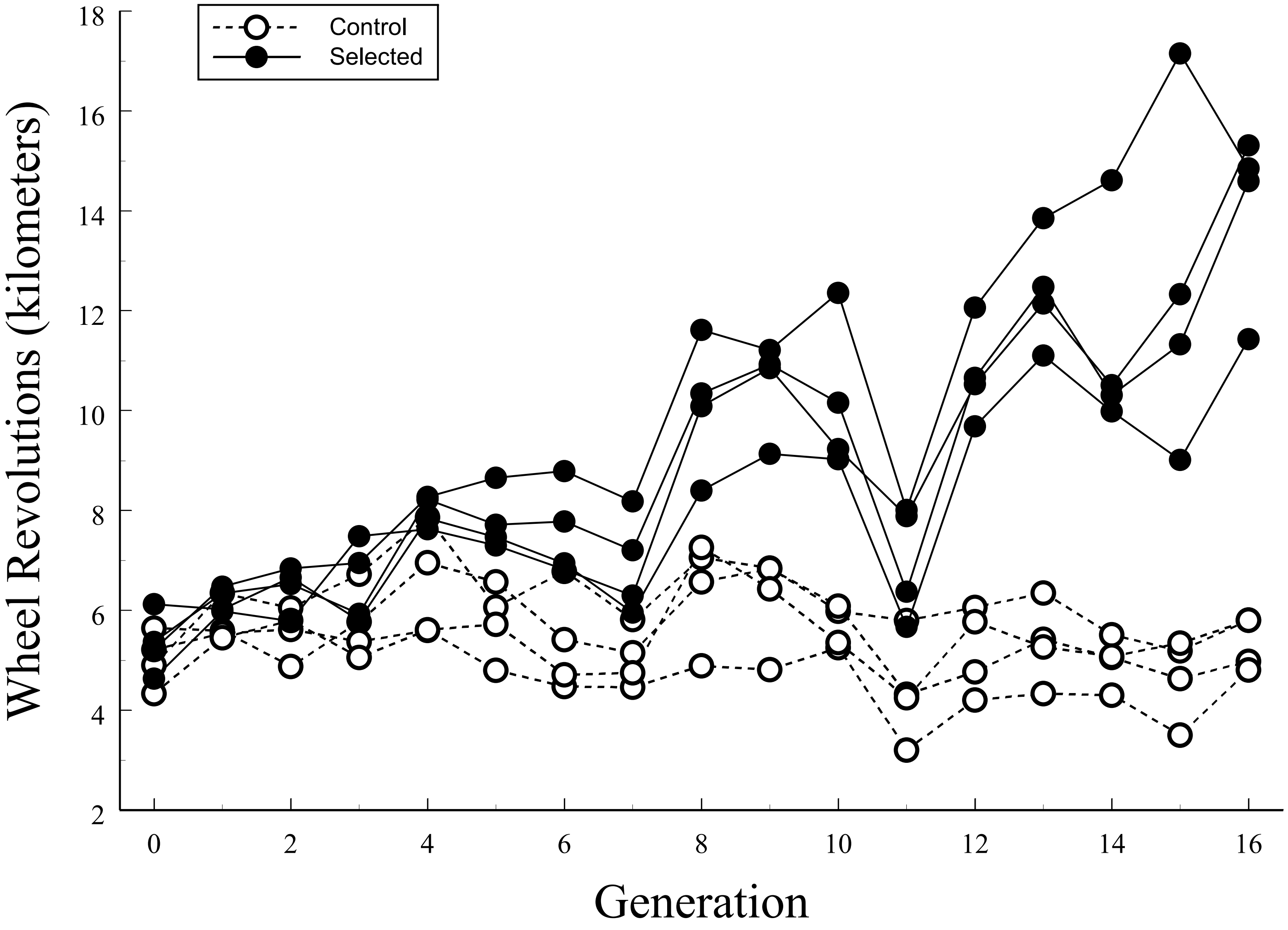
$$R = h^2S$$

$$\mathbf{R = V_A(s/V_P)}$$





Mean of Days 5 + 6 in Females



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