

# Basics of Quantitative Genetics

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# Background

- ▶ Central Dogma of Molecular Biology

- Genotypes are the basis for phenotypic expression

- ▶ Start with simple model

- one locus that affects quantitative trait

# Population

Population (N = 10)

$$\frac{G_1}{G_1}$$

$$\frac{G_1}{G_2}$$

$$\frac{G_2}{G_2}$$

$$\frac{G_2}{G_2}$$

$$\frac{G_1}{G_1}$$

$$\frac{G_2}{G_1}$$

$$\frac{G_1}{G_1}$$

$$\frac{G_1}{G_1}$$

$$\frac{G_2}{G_2}$$

$$\frac{G_2}{G_1}$$

# Terminology

- ▶ **alleles**: variants occurring at a given genetic Locus
- ▶ **bi-allelic**: only two alleles, e.g.,  $G_1$  and  $G_2$  at a given locus  $G$  in population
- ▶ **genotype**: combination of two alleles at locus  $G$  in an individual
- ▶ **homozygous**: genotypes  $G_1G_1$  and  $G_2G_2$  where both alleles identical
- ▶ **heterozygous**: genotype  $G_1G_2$  different alleles

# Frequencies in Example Population

► **genotype frequencies**

$$f(G_1 G_1) = \frac{4}{10} = 0.4$$

$$f(G_1 G_2) = \frac{3}{10} = 0.3$$

$$f(G_2 G_2) = \frac{3}{10} = 0.3$$

► **allele frequencies**

$$f(G_1) = f(G_1 G_1) + \frac{1}{2} * f(G_1 G_2) = 0.55$$

$$f(G_2) = f(G_2 G_2) + \frac{1}{2} * f(G_1 G_2) = 0.45$$

# Hardy-Weinberg Equilibrium

- ▶ **allele frequencies**

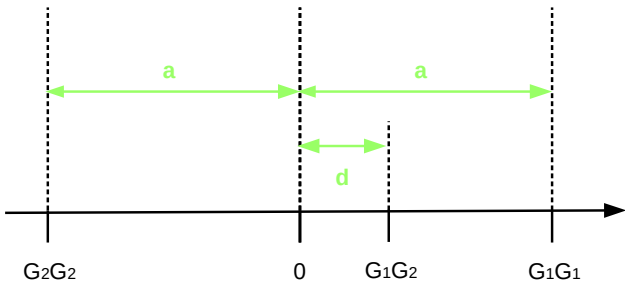
$$f(G_1) = p, f(G_2) = q = 1 - p$$

- ▶ **genotype frequencies**

Alleles	$G_1$	$G_2$
$G_1$	$f(G_1 G_1) = p^2$	$f(G_1 G_2) = p * q$
$G_2$	$f(G_1 G_2) = p * q$	$f(G_2 G_2) = q^2$

$$f(G_1 G_1) = p^2, f(G_1 G_2) = 2pq, f(G_2 G_2) = q^2$$

# Genotypic Values



# Population Mean

- Expected value of genotypic value  $V$  as discrete random variable

$$\begin{aligned}\mu &= V_{11} * f(G_1 G_1) + V_{12} * f(G_1 G_2) + V_{22} * f(G_2 G_2) \\ &= a * p^2 + d * 2pq + (-a) * q^2 \\ &= (p - q)a + 2pqd\end{aligned}$$



## Breeding Values Definition

The breeding value of an animal  $i$  is defined as two times the difference between the mean value of offsprings of animal  $i$  and the population mean.

## Derivation of Breeding value for $G_1 G_1$

	Mates of $S$	
	$f(G_1) = p$	$f(G_2) = q$
Parent $S$		
$f(G_1) = 1$	$f(G_1 G_1) = p$	$f(G_1 G_2) = q$

## Computation of Breeding value for $G_1 G_1$

$$\mu_{11} = p * a + q * d$$

The breeding value  $BV_{11}$  corresponds to

$$\begin{aligned} BV_{11} &= 2 * (\mu_{11} - \mu) \\ &= 2 (pa + qd - [(p - q)a + 2pqd]) \\ &= 2 (pa + qd - (p - q)a - 2pqd) \\ &= 2 (qd + qa - 2pqd) \\ &= 2 (qa + qd(1 - 2p)) \\ &= 2q (a + d(1 - 2p)) \\ &= 2q (a + (q - p)d) \end{aligned}$$

## Computation of Breeding value for $G_2G_2$

$$\mu_{22} = pd - qa$$

The breeding value  $BV_{22}$  corresponds to

$$\begin{aligned} BV_{22} &= 2 * (\mu_{22} - \mu) \\ &= 2 (pd - qa - [(p - q)a + 2pqd]) \\ &= 2 (pd - qa - (p - q)a - 2pqd) \\ &= 2 (pd - pa - 2pqd) \\ &= 2 (-pa + p(1 - 2q)d) \\ &= -2p(a + (q - p)d) \end{aligned}$$

## Computation of Breeding value for $G_1 G_2$

$$\mu_{12} = 0.5pa + 0.5d - 0.5qa = 0.5[(p - q)a + d]$$

The breeding value  $BV_{12}$  corresponds to

$$\begin{aligned} BV_{12} &= 2 * (\mu_{12} - \mu) \\ &= 2(0.5(p - q)a + 0.5d - [(p - q)a + 2pqd]) \\ &= 2(0.5pa - 0.5qa + 0.5d - pa + qa - 2pqd) \\ &= 2(0.5(q - p)a + (0.5 - 2pq)d) \\ &= (q - p)a + (1 - 4pq)d \\ &= (q - p)a + (p^2 + 2pq + q^2 - 4pq)d \\ &= (q - p)a + (p^2 - 2pq + q^2)d \\ &= (q - p)a + (q - p)^2d \\ &= (q - p)[a + (q - p)d] \end{aligned}$$

## Summary of Breeding Values

Genotype	Breeding Value
$G_1 G_1$	$2q\alpha$
$G_1 G_2$	$(q - p)\alpha$
$G_2 G_2$	$-2p\alpha$

with  $\alpha = a + (q - p)d$

## Allele Substitution

$$\begin{aligned}BV_{12} - BV_{22} &= (q - p)\alpha - (-2p\alpha) \\&= (q - p)\alpha + 2p\alpha \\&= (q - p + 2p)\alpha \\&= (q + p)\alpha \\&= \alpha\end{aligned}$$

$$\begin{aligned}BV_{11} - BV_{12} &= 2q\alpha - (q - p)\alpha \\&= (2q - (q - p))\alpha \\&= \alpha\end{aligned}$$

## Dominance Deviation I

$$\begin{aligned}V_{11} - BV_{11} &= a - 2q\alpha \\&= a - 2q[a + (q - p)d] \\&= a - 2qa - 2q(q - p)d \\&= a(1 - 2q) - 2q^2d + 2pqd \\&= [(p - q)a + 2pqd] - 2q^2d \\&= \mu + D_{11}\end{aligned}$$



## Dominance Deviation II

$$\begin{aligned}V_{12} - BV_{12} &= d - (q - p)\alpha \\&= d - (q - p)[a + (q - p)d] \\&= [(p - q)a + 2pqd] + 2pqd \\&= \mu + D_{12}\end{aligned}$$

$$\begin{aligned}V_{22} - BV_{22} &= -a - (-2p\alpha) \\&= -a + 2p[a + (q - p)d] \\&= [(p - q)a + 2pqd] - 2p^2d \\&= \mu + D_{22}\end{aligned}$$

## Summary of Values

Genotype $G_i G_j$	genotypic value $V_{ij}$	Breeding Value $BV_{ij}$	Dominance Deviation $D_{ij}$
$G_1 G_1$	$a$	$2q\alpha$	$-2q^2d$
$G_1 G_2$	$d$	$(q - p)\alpha$	$2pqd$
$G_2 G_2$	$-a$	$-2p\alpha$	$-2p^2d$

## Decomposition of Genotypic Values

$$V_{ij} = \mu + BV_{ij} + D_{ij}$$

## Variances

$$\text{Var}[X] = \sum_{x_i \in \mathcal{X}} (x_i - \mu_X)^2 * f(x_i)$$

where  $\mathcal{X}$ : set of all possible  $x$ -values  
 $f(x_i)$  probability that  $x$  assumes the value of  $x_i$   
 $\mu_X$  expected value  $E[X]$  of  $X$

## Variance Computation

$$\begin{aligned}\sigma_G^2 = Var[V] &= (V_{11} - \mu)^2 * f(G_1 G_1) \\ &+ (V_{12} - \mu)^2 * f(G_1 G_2) \\ &+ (V_{22} - \mu)^2 * f(G_2 G_2)\end{aligned}$$

where  $\mu = (p - q)a + 2pqd$  the population mean.

## Simplification

$$\begin{aligned}\sigma_G^2 = \text{Var}[V] &= (BV_{11} + D_{11})^2 * f(G_1 G_1) \\ &\quad + (BV_{12} + D_{12})^2 * f(G_1 G_2) \\ &\quad + (BV_{22} + D_{22})^2 * f(G_2 G_2)\end{aligned}$$

## Result

$$\begin{aligned}\sigma_G^2 &= 2pq\alpha^2 + (2pqd)^2 \\ &= \sigma_A^2 + \sigma_D^2\end{aligned}$$

## Two and more Loci

Two loci  $G$  and  $H$  have an effect on the same quantitative trait.

Genotype $G_i G_j H_k H_l$	genotypic value $V_{ijkl}$	Breeding Value $BV_{ijkl}$	Dominance $D_{ijkl}$	Epistasis $I_{ijkl}$
$G_1 G_1 H_1 H_1$	$V_{1111}$	$BV_{1111}$	$D_{1111}$	$I_{1111}$
$G_1 G_2 H_1 H_1$				
$G_2 G_2 H_1 H_1$				
...				

Because breeding values are additive

$$BV_{ijkl} = BV_{ij} + BV_{kl}$$