Basics of Quantitative Genetics

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Background

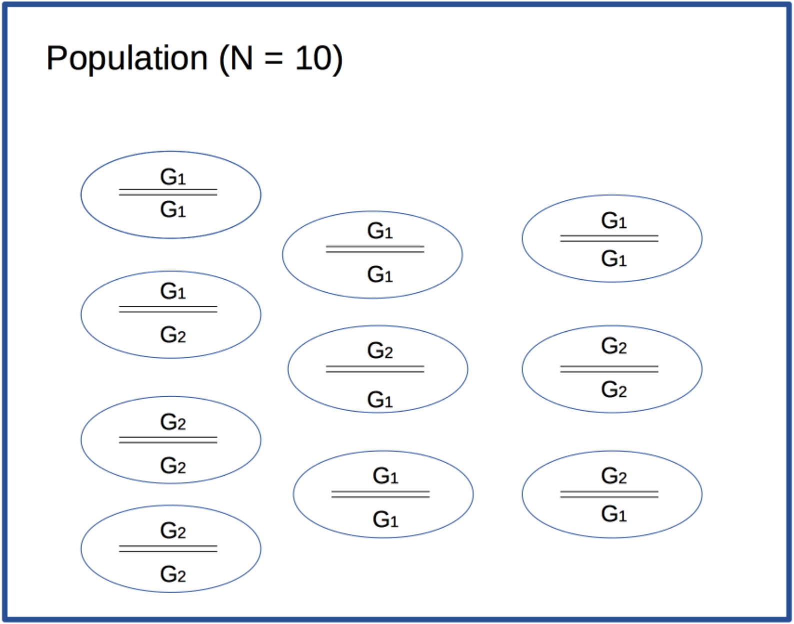
- Central Dogma of Molecular Biology

→ Genotypes are the basis for phenotypic expression

- Start with simple model

→ one locus that affects quantitative trait

Population


Population (N = 10)
G_1 / G_1
G_1 / G_2
G_2 / G_2
G_2 / G_2
G_1 / G_1
G_2 / G_1
G_1 / G_1
G_1 / G_1
G_2 / G_2
G_2 / G_1

Terminology

- **alleles**: variants occuring 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**

$$f(G_1G_1) = \frac{4}{10} = 0.4$$
$$f(G_1G_2) = \frac{3}{10} = 0.3$$
$$f(G_2G_2) = \frac{3}{10} = 0.3$$

- **allele frequencies**

$$f(G_1) = f(G_1G_1) + \frac{1}{2} * f(G_1G_2) = 0.55$$
$$f(G_2) = f(G_2G_2) + \frac{1}{2} * f(G_1G_2) = 0.45$$

Hardy-Weinberg Equilibrium

- **allele frequencies**

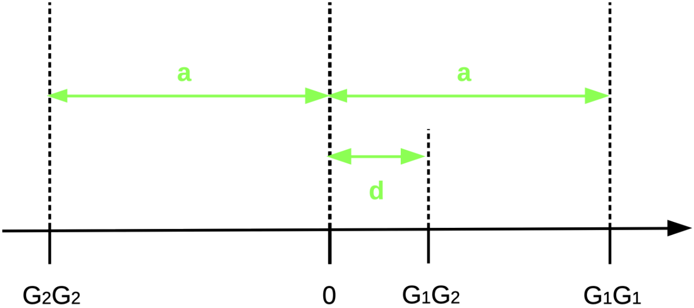
$$f(G_1) = p,\ f(G_2) = q = 1 - p$$

- **genotype frequencies**

Alleles	G_1	G_2
G_1	$f(G_1G_1) = p^2$	$f(G_1G_2) = p * q$
G_2	$f(G_1G_2) = p * q$	$f(G_2G_2) = q^2$

$$f(G_1G_1) = p^2,\ f(G_1G_2) = 2pq,\ f(G_2G_2) = q^2$$

Genotypic Values



Population Mean

- Expected value of genotypic value V as discrete random variable

$$\begin{aligned}
\mu &= V_{11} * f(G_1G_1) + V_{12} * f(G_1G_2) + V_{22} * f(G_2G_2) \\
&= a * p^2 + d * 2pq + (-a) * q^2 \\
&= (p-q)a + 2pqd
\end{aligned}$$

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_1G_1

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

The breeding value BV_{11} corresponds to

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

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 $G_1 G_2$

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

The breeding value BV_{12} corresponds to

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

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

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

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

Dominance Deviation I

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

Dominance Deviation II

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

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

Summary of Values

Genotype G_iG_j	genotypic value V_{ij}	Breeding Value BV_{ij}	Dominance Deviation D_{ij}
G_1G_1	a	$2q\alpha$	$-2q^2d$
G_1G_2	d	$(q-p)\alpha$	$2pqd$
G_2G_2	$-a$	$-2p\alpha$	$-2p^2d$

Decomposition of Genotypic Values

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

Variances

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

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

Variance Computation

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

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

Simplification

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

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

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