Basics of Quantitative Genetics

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2022-09-30

Background

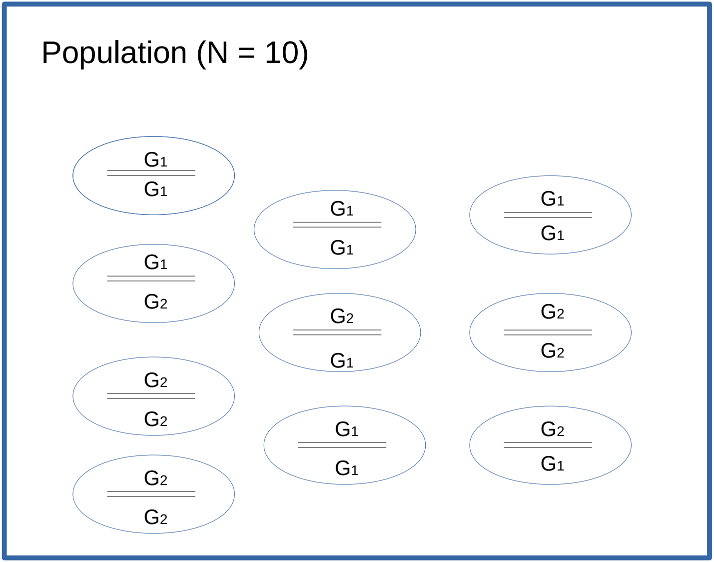
- Central Dogma of Molecular Biology

→ 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 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**

$$f(G_1 G_1) = \frac{4}{10} = 0.4$$
$$f(G_1 G_2) = \frac{3}{10} = 0.3$$
$$f(G_2 G_2) = \frac{3}{10} = 0.3$$

- **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**

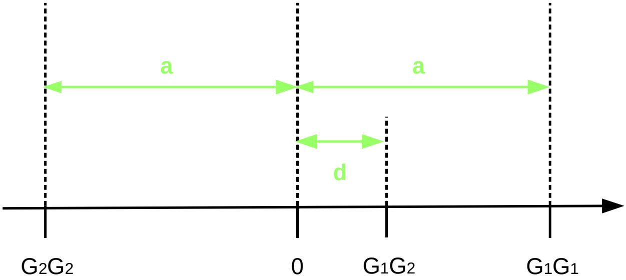
$$f(G_1) = p,\ f(G_2) = q = 1 - p$$

- **genotype frequencies**

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

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

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

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

Computation of Breeding value for G_1G_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_1G_1	$2q\alpha$
G_1G_2	$(q-p)\alpha$
G_2G_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 having an effect on the same quantitative trait.
- Effect of one locus can have an influence on the effect of the other locus

$\rightarrow$ **Interaction** between loci.

- Interaction is quantified by

$$I_{GH} = V - V_G - V_H$$

where V is the total genotypic value, V_G and V_H correspond to the genotypic values due to loci G and H, respectively

Decomposition and Collecting Terms

- Genotypic values can be decomposed as

$$
\begin{aligned}
V_G &= \mu_G + BV_G + D_G \\
V_H &= \mu_H + BV_H + D_H
\end{aligned}
$$

- Collecting terms leads to

$$V = V_G + V_H + I_{GH} = \mu + U + D + I$$

with $\mu = \mu_G + \mu_H$, $U = BV_G + BV_H$, $D = D_G + D_H$ and $I = I_{GH}$

- Can be generalized to more than two loci.

More Than Two Loci

- Genotypic value V influenced by an unknown number of loci: $A, B, C, \ldots,$
- Decomposition of V

$$V = V_A + V_B + V_C + \ldots + I_{ABC\ldots}$$

where $I_{ABC\ldots}$ is a generic Interaction term which we do not specify further here.

Decomposition

- Genotypic value of single loci

$$V_A = V_{A_iA_j} = \mu_A + BV_{A_iA_j} + D_{A_iA_j}$$

$$V_B = V_{B_iB_j} = \mu_B + BV_{B_iB_j} + D_{B_iB_j}$$

$$V_C = V_{C_iC_j} = \mu_C + BV_{C_iC_j} + D_{C_iC_j}$$

Collecting Terms

- for a given animal k, μ, BV and D terms are collected

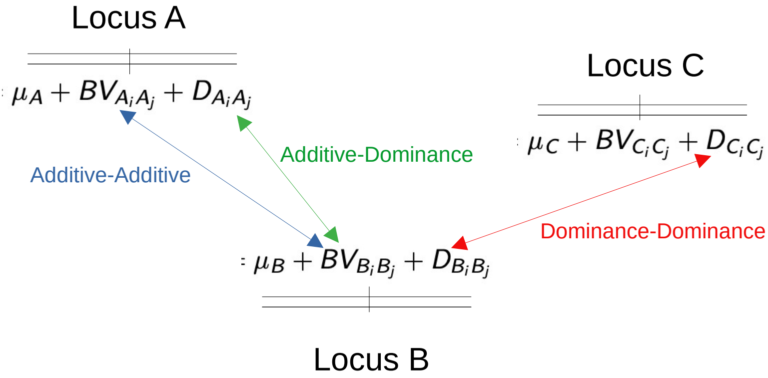
$$\mu_k = \mu_A + \mu_B + \mu_C + \dots$$

$$U_k = BV_k = BV_{A_iA_j} + BV_{B_iB_j} + BV_{C_iC_j} + \dots$$

$$D_k = D_{A_iA_j} + D_{B_iB_j} + D_{C_iC_j} + \dots$$

Interactions

Interaction effects ($I_{ABC\ldots}$) can occur between different genetic components



Locus A

$\mu_A + BV_{A_iA_j} + D_{A_iA_j}$

Locus C

$\mu_C + BV_{C_iC_j} + D_{C_iC_j}$

Additive-Additive

Additive-Dominance

Dominance-Dominance

$\mu_B + BV_{B_iB_j} + D_{B_iB_j}$

Locus B

Phenotype

- Including phenotypic observations y
- Central Dogma of Molecular Biology
- Decomposition

$$y = V + E$$

where V is the genotypic value and E is the non-genetic or environmental effect. (Before: $P = G + E$)

- Insert decomposition of V as shown above

Decomposition of Phenotype

- Insert $V = V_A + V_B + V_C + \ldots + I_{ABC\ldots}$ into $y = V + E$

$$y = V + E = V_A + V_B + V_C + \ldots + I_{ABC\ldots} + E$$

$$= (\mu_A + BV_{A_iA_j} + D_{A_iA_j}) + (\mu_B + BV_{B_iB_j} + D_{B_iB_j})$$

$$+(\mu_C + BV_{C_iC_j} + D_{C_iC_j}) + ...I_{ABC\ldots} + E$$

Collecting terms

$$= (\mu_A + \mu_B + \mu_C + ...) + (BV_{A_iA_j} + BV_{B_iB_j} + BV_{C_iC_j} + ...)$$

$$+(D_{A_iA_j} + D_{B_iB_j} + D_{C_iC_j} ...) + I_{ABC...} + E$$

$$= \mu + BV + D + I_{ABC...} + E = \mu + BV + E^* = \mu + U + E^*$$