	LOUISIANA STATE UNIVERSITY **College of Agriculture** **School of Plant, Environmental, and Soil Sciences** **AGRO 7075 Prediction-based Breeding**	

Variance and Genetic Effects

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Non-inbred populations

- Population = a pool of shared alleles
- Only the allele is passed to the offspring, not the genotype
- **Allele frequencies**
- $B = f(B) = p$
- $= p^2 + ½(2pq)$
- $= p^2 + pq$
- $= p^2 + p(1-p)$
- $= p^2 + p - p^2$
- $= p$
- $b = f(b) = q$
- $= q^2 + ½ 2pq)$
- $= q^2 + pq$
- $= q^2 + q(1-q)$
- $= q^2 + q - q^2$
- $= q$
- **Under HWE these frequencies are kept constant**
- **Otherwise, with just one random mating this equilibrium is reached again**

Genotype	*f*
BB	p^2
Bb	$2pq$
bb	q^2

Inbred populations

- **Inbred populations**
- Alleles identical by descendent (**IBD**) – copies of a shared ancestral
- Alleles identical by state (**IBS**) – same allele, but different origin

- **Inbreeding coefficient**
- $F = P\,(B_i \equiv B_j)$
- $F = ¼ + ¼ = ½$

Allele	B	b
B	BB (1/4) IBD	Bb (1/4)
b	bB (1/4)	bb (1/4) IBD

- **Probability of IBD**
- It is equal of the allele frequency times the inbreeding rate
- $P(BB) = Fp$
- $P(bb) = Fq$

- **Non-inbred genotypes** = 1 - F
- **Inbred genotypes** = F

Inbred populations

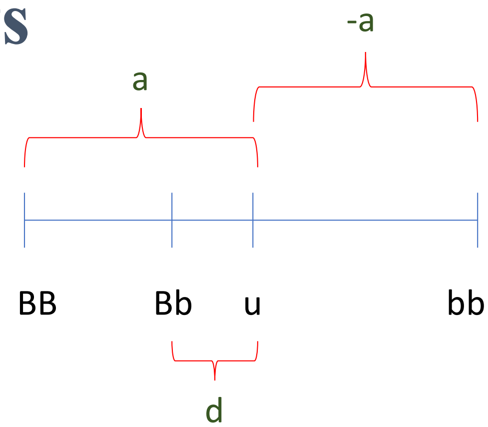
- **IBD** **IBS**
- $= F(BB + bb) + (1 - F)(BB + Bb + bb)$
- $= F(pBB + qbb) + (1 - F)(p^2BB + 2pqBb + q^2bb)$
- $= FpBB + Fqbb + p^2BB + 2pqBb + q^2bb - Fp^2BB - 2FpqBb - Fq^2bb$
- $= BB[Fp + p^2 – Fp^2] + Bb[2pq – 2Fpq] + bb[Fq + q^2 - Fq^2]$
- $= BB[p^2 + Fp – Fp(1-q)] + Bb[2pq – 2pqF] + bb[q^2 + Fq – Fq(1-p)]$

- **Then, for any F**
- $= BB[p^2 + pqF] + Bb[2pq – 2pqF] + bb[q^2 + pqF]$

- **F = 1**
- $p^2 + pqF$
- $p^2 + pq$
- $p^2 + p(1-p)$
- $p^2 + p - p^2 = p$

Genotype	*f*	*F=0*	*F=1*
BB	$p^2 + pqF$	p^2	p
Bb	$2pq – 2pqF$	2pq	0
bb	$q^2 + pqF$	q^2	q

Genotypes and genic effects



- Intra population - assuming HWE
- $\boldsymbol{\alpha}$ = female *i* and male *j* allele effects at the *k* locus
- δ = interaction between alleles *i* and *j*
- The sum of the $\boldsymbol{\alpha}$ over *k loci* means *Breeding value (BV)*
- Substitution allele effect
- $\boldsymbol{\alpha}_B = u_B - u_{pop}$
- $\boldsymbol{\alpha}_b = u_b - u_{pop}$
- Crosses
- BB x population = u_B
- bb x population = u_b
- $u_B = pa + qd$
- $u_b = q(-a) + pd$

- $u_{pop} = p^2a + q^2(-a) + 2pqd$
- $= \mathbf{(p^2 - q^2)}a + 2pqd$
- $= (p - q)a + 2pqd$

- $\mathbf{(p^2 - q^2)} = (1 - q)^2 - q^2 = 1 - 2q + q^2 - q^2 = p + q - 2q = p - q$

$$y_i = u + g_i + g_j + s_{ij}$$

$$G_{ij} = u + \alpha_i + \alpha_j + \delta_{ij}$$

Genotype	*f*	*VG*
BB	p^2	a
Bb	2pq	d
bb	q^2	-a

Genotype	*f*	*Mean*	*Dominance*
BB	p^2	$\boldsymbol{\alpha}_B + \boldsymbol{\alpha}_B$	δ_{BB}
Bb	2pq	$\boldsymbol{\alpha}_B + \boldsymbol{\alpha}_b$	δ_{Bb}
bb	q^2	$\boldsymbol{\alpha}_b + \boldsymbol{\alpha}_b$	δ_{bb}

Substitution allele effect

- $\boldsymbol{\alpha}_B = u_B - u_{pop}$
- $= pa + qd - [(p - q)a + 2pqd]$
- $= pa + qd - pa + qa - 2pqd$
- $= qa + qd - 2pqd$
- $= q[a + (1 - 2p)d]$
- $= q[a + (q + p - 2p)d]$
- $= q[a + (q - p)d]$
- $= q\boldsymbol{\alpha}$

- $\boldsymbol{\alpha}_b = u_b - u_{pop}$
- $= -qa + pd - [(p - q)a + 2pqd]$
- $= -qa + pd - pa + qa - 2pqd$
- $= pd - pa - 2pqd$
- $= -p[a - d + 2qd]$
- $= -p[a(2q - 1)d]$
- $= -p[a(2q - p + q)d]$
- $= -p[a + (q - p)d]$
- $= -p\boldsymbol{\alpha}$

Dominance effect

- $BB = u + 2\boldsymbol{\alpha}_B + \mathcal{S}_{BB} = a$
- $\mathcal{S}_{BB} = a - u - 2\boldsymbol{\alpha}_B$
- $= a - [(p - q)a + 2pqd] - 2[q[a + (q - p)d]$
- $= a - pa + qa - 2pqd - 2qa - 2q(q - p)d$
- $= a - pa - qa - 2pqd - 2q^2d + 2pqd$
- $= a - pa - qa - 2q^2d$
- $= a(1 - p - q) - 2q^2d$
- $= a(p + q - p - p) - 2q^2d$
- $= -2q^2d$
- $bb = u + 2\boldsymbol{\alpha}_b + \mathcal{S}_{bb} = -a$
- $\mathcal{S}_{bb} = -a - u - 2\boldsymbol{\alpha}_b$
- $= -a - [(p - q)a + 2pqd] - 2 [-p[a + (q - p)d]$
- $= -a - pa + qa - 2pqd + 2pa + 2p(q - p)d$
- $= -a + pa + qa - 2pqd - 2p^2d + 2pqd$
- $= - a + pa + qa - 2p^2d$
- $= a(p + q - 1) - 2p^2d$
- $= a(p + q - p - q) - 2p^2d$
- $= -2p^2d$

- $Bb = u + \boldsymbol{\alpha}_B + \boldsymbol{\alpha}_b + \mathcal{S}_{Bb} = d$
- $\mathcal{S}_{Bb} = d - u - \boldsymbol{\alpha}_B - \boldsymbol{\alpha}_b$
- $= d - [(p - q)a + 2pqd] - [q[a + (q - p)d] - [-p[a + (q - p)d]$
- $= d - pa + qa + 2pqd - qa - q(q - p)d + pa - p(q - p)d$
- $= d - 2pqd - q(q - p)d - p(q - p)d$
- $= d - 2pqd - q^2d + pqd - p^2d + pqd$
- $= d - q^2d - p^2d$
- $= d(1 - q^2 - p^2)$
- $= d(1 - (1 - p)^2 - p^2)$
- $= d(1 - (1 + p^2 + 2p) - p^2)$
- $= d(1 - 1 - p^2 - 2p - p^2)$
- $= d(2p - 2p^2)$
- $= 2d[p - p(1 - q)]$
- $= 2d[p - p + pq]$
- $= 2d[pq]$
- $= 2pqd$

Genotype	*f*	*Mean*	*Dominance*
BB	p^2	$\boldsymbol{\alpha}_B+\boldsymbol{\alpha}_B$	$\mathcal{S}_{BB}$
Bb	2pq	$\boldsymbol{\alpha}_B+\boldsymbol{\alpha}_b$	$\mathcal{S}_{Bb}$
bb	q^2	$\boldsymbol{\alpha}_b+\boldsymbol{\alpha}_b$	$\mathcal{S}_{bb}$

Substitution allele effect

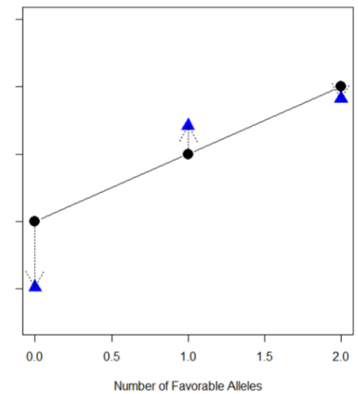
- **α** is the slope of the regression line
- Regression coefficient – ***b***

$$b = \frac{COV(x,y)}{V_x}$$

Genotype	*f*	*Alleles x*	*VG y*
BB	p^2	2	a
Bb	2pq	1	d
bb	q^2	0	-a

$$\sigma^2 = \sum_i f_i X_i^{\,2} - \left(\sum_i f_i X_i\right)^2 \qquad COV_{xy} = \sum_i f_i X_i Y_i - \left(\sum_i f_i X_i \,.\, \sum_i f_i Y_i\right)$$

- Thus, the variance of x is given by:
- $p^2(2^2) + 2pq(1^2) + q^2(0^2) = 4p^2 + 2pq$
- $[p^2(2) + 2pq(1) + q^2(0)]^2 = [2p^2 + 2pq]^2 = [2p^2 + 2p(1 – p)]^2 = [2p^2 + 2p – 2p^2]^2 = [2p]^2 = 4p^2$
- $Vx = 4p^2 + 2pq - 4p^2 = 2pq$
- and the covariance by
- 1) $p^2(a)(2) + 2pq(d)(1) + q^2(-a)(0) = 2p^2a + 2pqd$
- 2) $p^2(2) + 2pq(1) + q^2(0) = 2p^2 + 2pq = 2p$
- 3) $p^2(a) + 2pq(d) + q^2(-a) = p^2a + 2pqd – q^2a = (p^2 – q^2)a + 2pqd = (p – q)a + 2pqd$
- 2*3) $2p * (p^2 – q^2)a + 2pqd = 2p(p - q)a + 4p^2qd$
- Finally, $COV(x, y) = 2p^2a + 2pqd - 2p(p - q)a + 4p^2qd = 2pq[a + (q – p)d]$



$$b = \frac{COV(x,y)}{V_x} = \frac{2pq[a + (q – p)d]}{2pq} = a + (q – p)d = \alpha$$

Additive variance

- $V(X) = E[X - E(X)]^2$

$$G_{ij} = u + \propto_i + \propto_j + \delta_{ij}$$

- $Vg = E[G_{ij} - E(G_{ij})]^2$
- $= E[u + \boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j + \boldsymbol{S}_{ij} - u]^2$
- $= E[\boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j + \boldsymbol{S}_{ij}]^2$
- $= E[\boldsymbol{\alpha}_i]^2 + E[\boldsymbol{\alpha}_j]^2 + E[\boldsymbol{S}_{ij}]^2 + \ldots$
- $= E[\boldsymbol{\alpha}_i]^2 + E[\boldsymbol{\alpha}_j]^2 + E[\boldsymbol{S}_{ij}]^2$

- Additive variance = variance of the average allele effects

- $= E[\boldsymbol{\alpha}_i]^2 = E[p_i(\boldsymbol{\alpha}_i)^2 - E(p_i\boldsymbol{\alpha}_i)]^2$
- $= E[p_i(\boldsymbol{\alpha}_i)^2 - 0]^2$
- $= \sum p_i(\boldsymbol{\alpha}_i)^2 = ½\ Va$

- $= E[\boldsymbol{\alpha}_j]^2 = E[p_i(\boldsymbol{\alpha}_j)^2 - E(p_i\boldsymbol{\alpha}_j)]^2$
- $= E[p_i(\boldsymbol{\alpha}_j)^2 - 0]^2$
- $= \sum p_i(\boldsymbol{\alpha}_j)^2 = ½\ Va$

$$\sigma_A^2 = 2\sum_i p_i(\alpha_i)^2$$

- $Va = 2.p.\boldsymbol{\alpha}_B{}^2 + 2.q.\boldsymbol{\alpha}_b{}^2$
- $= 2.p.(q\boldsymbol{\alpha})^2 + 2.q.(-p\boldsymbol{\alpha})^2$
- $= 2pq^2\boldsymbol{\alpha}^2 + 2qp^2\boldsymbol{\alpha}^2$
- $= 2pq\boldsymbol{\alpha}^2(q + p)$
- $= 2pq\boldsymbol{\alpha}^2$
- $= 2pq[a + (q - p)d]^2$

- $A = \boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j = E(\boldsymbol{\alpha}_B + \boldsymbol{\alpha}_b) = 0$

- $E(A) = E(\boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j) = E(\boldsymbol{\alpha}_i) + E(\boldsymbol{\alpha}_j)$
- $p_i.\boldsymbol{\alpha}_i + p_j\boldsymbol{\alpha}_j$
- $p_i(\boldsymbol{\alpha}_B) + p_j(\boldsymbol{\alpha}_b)$
- $p(q\boldsymbol{\alpha}) + q(-p\boldsymbol{\alpha})$
- $p(q\boldsymbol{\alpha}) + q(-p\boldsymbol{\alpha})$
- $pq\boldsymbol{\alpha} - pq\boldsymbol{\alpha} = 0$

Dominance

- Dominance variance = interaction between allele effects within a locus

$$G_{ij} = u + \propto_i + \propto_j + \delta_{ij}$$

Genotype	*f*	*value*	*Dominance*
BB	p^2	$-2q^2d$	$\mathcal{S}_{BB}$
Bb	$2pq$	$2pqd$	$\mathcal{S}_{Bb}$
bb	q^2	$-2p^2d$	$\mathcal{S}_{bb}$

- $= E[\mathcal{S}_{ij}]^2 = E[p_i(\mathcal{S}_{ij})^2 - E(p_i\mathcal{S}_{ij})]^2$
- $= E[p_i(\mathcal{S}_{ij})^2 - 0]^2$
- $= p_i(\mathcal{S}_{ij})^2 =$ Vd

$$\sigma_D^2 = \sum_i p_i p_j (S_{ij})^2$$

- $Vd = p^2.\mathcal{S}_{BB}{}^2 + 2pq.\mathcal{S}_{Bb}{}^2 + q^2.\mathcal{S}_{bb}{}^2$
- $= p^2(-2q^2d)^2 + 2pq(2pqd)^2 + q^2(-2p^2d)^2$
- $= p^2(4q^4d^2) + 2pq(4p^2q^2d^2) + q^2(4p^4d^2)$
- $= 4p^2q^2d^2\,(q^2 + 2pq + p^2)$
- $= 4p^2q^2d^2\,(p + q)^2$
- $= (2pqd)^2$

- $E(D) = \sum_{ij}(p_i p_j S_{ij})$
- $= p^2.\mathcal{S}_{BB} + 2pq.\mathcal{S}_{Bb} + q^2.\mathcal{S}_{bb}$
- $= p^2(-2q^2d) + 2pq(2pqd) + q^2(-2p^2d)$
- $= -2p^2q^2d + 4p^2q^2d + 2p^2q^2d$
- $= 0$

Mean in inbred populations

Genotype	*f*	*F=0*	*F=1*
BB	p^2+pqF	p^2	p
Bb	2pq – 2pqF	2pq	0
bb	q^2+pqF	q^2	q

- **IBD** **IBS**
- = F(BB + bb) + (1-F)(BB + Bb + bb)
- = BB[p^2 + pqF] + Bb[2pq – 2pqF] + bb[q^2 + pqF]

$$G_{ij} = u + \alpha_i + \alpha_j + \delta_{ij}$$

- $E(G_{ij}) = F\sum_i p_i(u + \boldsymbol{\alpha}_i + \boldsymbol{\alpha}_i + \boldsymbol{S}_{ij}) + (1 - F)\sum_{ij} p_i p_j(u + \boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j + \boldsymbol{S}_{ij})$
- $= Fu + 2F\sum_i p_i\boldsymbol{\alpha}_i + F\sum_i p_i\boldsymbol{S}_{ii} + (1 - F)u + (1 - F)\sum_i p_i\boldsymbol{\alpha}_i + (1 - F)\sum_j p_j\boldsymbol{\alpha}_j + (1 - F)\sum_{ij} p_i pj \boldsymbol{S}_{ij}$
- $= Fu + (1 - F)u + (1 - F)\sum_i p_i\boldsymbol{S}_{ii}$
- $= u + F\sum_i p_i\boldsymbol{S}_{ii}$
- Mean + inbreeding depression (ID)
- $F\sum_i p_i\boldsymbol{S}_{ii} = Fp\boldsymbol{S}_{BB} + Fq\boldsymbol{S}_{bb}$
- $= Fp(-2q^2d) + Fq(-2p^2d)$
- $= F(-2pq^2d) + F(-2qp^2d)$
- $= -2pqdF$
- Thus,
- $u_F = u - 2pqdF$
- $u_F = (p - q)a + 2pqd - 2pqdF$

Variance in inbred populations

- $Vg = E[G_{ij} - E(G_{ij})]^2$
- $= E[u + \boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j + \boldsymbol{S}_{ij} - u - F\sum_i p_i \boldsymbol{S}_{ii}]^2$
- $= E[\boldsymbol{\alpha}_i + \boldsymbol{\alpha}_j + \boldsymbol{S}_{ij} - F\sum_i p_i \boldsymbol{S}_{ii}]^2$
- $= E[\boldsymbol{\alpha}_i]^2 + E[\boldsymbol{\alpha}_j]^2 + E[\boldsymbol{S}_{ij}]^2 + E(-F\sum_i p_i \boldsymbol{S}_{ii})^2 + dp$

- $= E[\boldsymbol{\alpha}_i]^2 = E[\sum p_i(\boldsymbol{\alpha}_i)^2 - E(p_i\boldsymbol{\alpha}_i)]^2$
- $= E[p_i(\boldsymbol{\alpha}_i)^2 - 0]^2$
- $= \sum p_i(\boldsymbol{\alpha}_i)^2 = ½\ Va$

- $= E[\boldsymbol{\alpha}_j]^2 = E[p_i(\boldsymbol{\alpha}_j)^2 - E(p_i\boldsymbol{\alpha}_j)]^2$
- $= E[p_i(\boldsymbol{\alpha}_j)^2 - 0]^2$
- $= \sum p_i(\boldsymbol{\alpha}_j)^2 = ½\ Va$

- $= E[\boldsymbol{S}_{ij}]^2 = (1 - F)\sum_{ij} p_i p_j(\boldsymbol{S}_{ij})^2 - F\sum_i p_i(\boldsymbol{S}_{ii})^2$
- non-inbred inbred
- $= (1 - F)Vd - F\sum_i p_i(\boldsymbol{S}_{ii})^2$

- $E(-F\sum_i p_i \boldsymbol{S}_{ii})^2 = (F\sum_i p_i \boldsymbol{S}_{ii})^2$

- $2E(\boldsymbol{\alpha}_i\boldsymbol{\alpha}_j) = 2(1 - F)E(\boldsymbol{\alpha}_i)E(\boldsymbol{\alpha}_j) + 2F\sum_i p_i(\boldsymbol{\alpha}_i)^2$
- $= 0 + 2F\sum p_i(\boldsymbol{\alpha}_i)^2$
- $= 2F\ ½\ Va = F Va$

- $2E(\boldsymbol{\alpha}_i\boldsymbol{S}_{ij}) = 2(1 - F)E(\boldsymbol{\alpha}_i)E(\boldsymbol{S}_{ij}) + 2F\sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii}$
- $= 0 + 2F\sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii}$

- $2E(\boldsymbol{\alpha}_i\boldsymbol{S}_{ij}) = 2(1 - F)E(\boldsymbol{\alpha}_j)E(\boldsymbol{S}_{ij}) + 2F\sum_j p_j \boldsymbol{\alpha}_j \boldsymbol{S}_{jj}$
- $= 0 + 2F\sum_j p_j \boldsymbol{\alpha}_j \boldsymbol{S}_{jj}$

- $2E(\boldsymbol{\alpha}_i \,.\, -F\sum_i p_i \boldsymbol{S}_{ii}) = 2E(\boldsymbol{\alpha}_i)(-F\sum_i p_i \boldsymbol{S}_{ii})$
- $= 0$

- $2E(\boldsymbol{\alpha}_j \,.\, -F\sum_j p_j \boldsymbol{S}_{ij}) = 2E(\boldsymbol{\alpha}_j)(-F\sum_j p_j \boldsymbol{S}_{ij})$
- $= 0$

Variance in inbred populations

- $2E(\boldsymbol{S}_{ij}\,.\, - F\sum_i p_i \boldsymbol{S}_{ii}) = (1 - F)E(\boldsymbol{S}_{ij})(- F\sum_i p_i \boldsymbol{S}_{ii}) + 2FE(\boldsymbol{S}_{ii})(- F\sum_i p_i \boldsymbol{S}_{ii})$
- $= 0 + (2F\sum_i p_i \boldsymbol{S}_{ii})(- F\sum_i p_i \boldsymbol{S}_{ii})$
- $= -2F^2(\sum_i p_i \boldsymbol{S}_{ii})^2$
- Finally,
- $Vg = ½\, Va + ½\, Va + (1 - F)Vd - F\sum_i p_i(\boldsymbol{S}_{ii})^2 + 2F\sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii} + 2F\sum_j p_j \boldsymbol{\alpha}_j \boldsymbol{S}_{jj} - 2F^2(\sum_i p_i \boldsymbol{S}_{ii})^2$
- $Vg = (1+F)Va + (1 - F)Vd + 2F \sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii} + 2F \sum_j p_j \boldsymbol{\alpha}_j \boldsymbol{S}_{jj} + (F\sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii})^2 - 2(F^2\sum_i p_i \boldsymbol{S}_{ii}{}^2)$
- $D_1 = ½\, (\sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii} + \sum_j p_i \boldsymbol{\alpha}_j \boldsymbol{S}_{jj}) = \sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii}$
- Covariance between additive and dominance effects in the homozygotes

- $Vg = (1+F)Va + (1 - F)Vd + 4FD_1 + F\sum_i p_i(\boldsymbol{S}_{ii})^2 - F^2(\sum_i p_i \boldsymbol{S}_{ii})^2$
- $Vg = (1+F)Va + (1 - F)Vd + 4FD_1 + F[\sum_i p_i(\boldsymbol{S}_{ii})^2 - (\sum_i p_i \boldsymbol{S}_{ii})^2] + F((1 - F)(\sum_i p_i \boldsymbol{S}_{ii})^2$

- D_2 = Variance due to the dominance effects in the homozygotes
- H = the square of the inbreeding depression

- $Vg = (1+F)Va + (1 - F)Vd + 4FD_1 + FD_2 + F(1 - F)H$

Variance at any level of inbreeding

- $Vg = (1 + F)Va + (1 - F)Vd + 4FD_1 + FD_2 + F(1 - F)H$
- $D_1 = COV(a,d)$
- $D_2 = V(S_{ii})$
- *H = the square of the inbreeding depression*

- F = 0
- $Vg = (1 + 0)Va + (1 - 0)Vd + 4.0.D_1 + 0D_2 + 0(1 - 0)H$
- $Vg = Va + Vd$

- F = 1
- $Vg = (1 + 1)Va + (1 - 1)Vd + 4.1.D_1 + 1D_2 + 1(1 - 1)H$
- $Vg = 2Va + 4D_1 + D_2$

- Inbred progenies = Normally, D_1 is negative, reducing the Vg
- On the other hand, the bigger F, the bigger Va

Mixed populations

- s = inbreeding rate
- $s = 2F / (1 + F)$
- $F = s / (2 - s)$

- $Vg = (1 + F)Va + (1 - F)Vd + 4FD_1 + FD_2 + F((1 - F)H$

$$Vg = \left(\frac{2}{2-s}\right)Va + \left(\frac{2-2s}{2s}\right)Vd + \left(\frac{4s}{2s}\right)D1 + \left(\frac{s}{2s}\right)D2 + \left[\frac{2(1-s)}{2s^2}\right]H$$

- *Considering two alleles*
- $Va = 2\sum p_i(\boldsymbol{\alpha}_i)^2 = 2pq\boldsymbol{\alpha}^2$
- $Vd = \sum_{ij} p_i p_j (\boldsymbol{S}_{ij})^2 = (2pqd)^2$
- $D_1 = \sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii} = 2pq(q - p)(a + (q - p)d)d = 2pq(q - p)\boldsymbol{\alpha}d$
- $D_2 = \sum_i p_i (\boldsymbol{S}_{ii})^2 - (\sum_i p_i \boldsymbol{S}_{ii})^2 = 4pqd^2(q - p)^2$
- $H = (\sum_i p_i \boldsymbol{S}_{ii})^2 = (2pqd)^2$

- Parametric space
- $Va \geq 0$
- $Vd \geq 0$
- $-\infty \leq D_1 \leq +\infty$
- $D_2 \geq 0$
- $H \geq 0$

D_1 and D_2

- $D_1 = \sum_i p_i \boldsymbol{\alpha}_i \boldsymbol{S}_{ii}$
- $= p\boldsymbol{\alpha}_B \boldsymbol{S}_{BB} + q\boldsymbol{\alpha}_b \boldsymbol{S}_{bb}$
- $= p(q\boldsymbol{\alpha})(-2q^2d) + q(-p\boldsymbol{\alpha})(-2p^2d)$
- $= 2pq^3\boldsymbol{\alpha}d + 2p^3q\boldsymbol{\alpha}d$
- $= -2pq(q - p)\boldsymbol{\alpha}d$

- $D_2 = \sum_i p_i(\boldsymbol{S}_{ii})^2 - (\sum_i p_i \boldsymbol{S}_{ii})^2$
- $= [p(-2q^2d)^2 + q(-2p^2d)^2] - [p(-2q^2d) + q(-2p^2d)]^2$
- $= [4pq^4d^2 + 4qp^4d^2] - [-2pq^2d - 2qp^2d)]^2$
- $= [4pqd^2(p^3 + q^3)] - [-2pqd(q + p)]^2$
- $= [4pqd^2(p^3 + q^3)] - 4p^2q^2d^2$
- $= 4pqd^2(p^3 + q^3 - pq)$
- $= 4pqd^2(p^3 + (1 - p)^3 - p(1 - p))$
- $= 4pqd^2(p^3 + (1 - p)^3 - p + p^2)$
- $= 4pqd^2(1 - 2p)^2$
- $= 4pqd^2(q - p)^2$