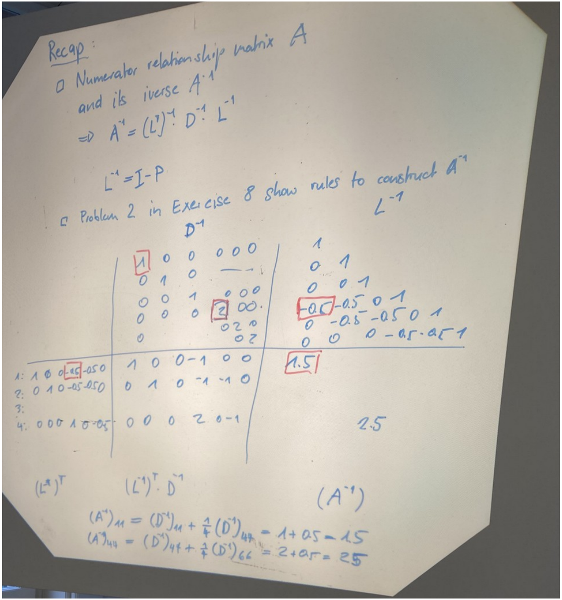
OHP Picture 1



Recap:

☐ Numerator relationship matrix A
and its iverse A^{-1}
$\Rightarrow A^{-1} = (L^T)^{-1} \cdot D^{-1} \cdot L^{-1}$

$L^{-1} = I - P$

☐ Problem 2 in Exercise 8 show rules to construct A^{-1}

D^{-1}

$\boxed{1}$ 0 0 0 0 0
0 1 0 ——→
0 0 1 0 0 0
0 0 0 $\boxed{2}$ 0 0
0 2 0
0 0 2

L^{-1}

1
0 1
0 0 1
$\boxed{-0.5}$ -0.5 0 1
0 -0.5 -0.5 0 1
0 0 0 -0.5 -0.5 1

1: 1 0 0 $\boxed{-0.5}$ -0.5 0
2: 0 1 0 -0.5 -0.5 0
3:
4: 0 0 0 1 0 -0.5

1 0 0 -1 0 0
0 1 0 -1 -1 0
0 0 0 2 0 -1

$\boxed{1.5}$

2.5

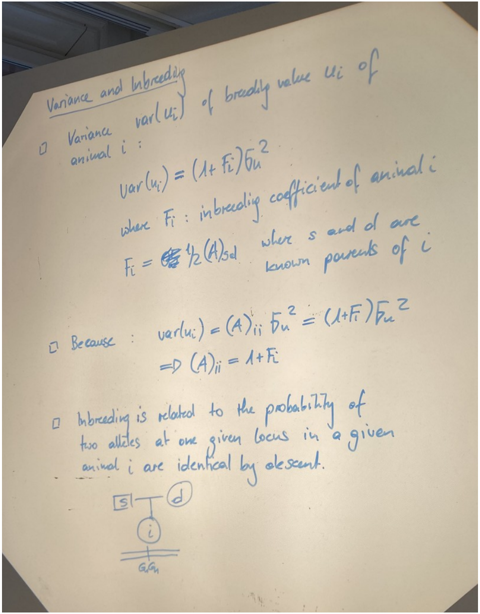
$(L^{-1})^T$

$(L^{-1})^T \cdot D^{-1}$

(A^{-1})

$(A^{-1})_{11} = (D^{-1})_{11} + \frac{1}{4}(D^{-1})_{44} = 1 + 0.5 = 1.5$
$(A^{-1})_{44} = (D^{-1})_{44} + \frac{1}{4}(D^{-1})_{66} = 2 + 0.5 = 2.5$

OHP Picture 2



Variance and Inbreeding

☐ Variance $var(u_i)$ of breeding value u_i of animal i:

$$var(u_i) = (1+F_i)\sigma_u^2$$

where F_i : inbreeding coefficient of animal i

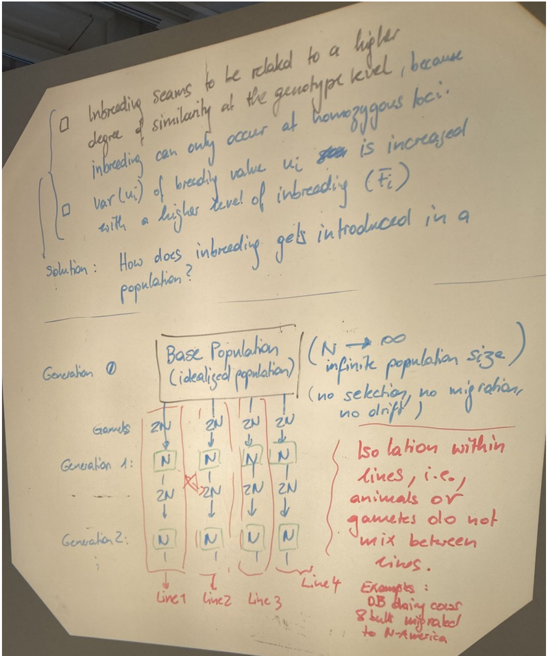
$F_i = \frac{1}{2}(A)_{sd}$ where s and d are known parents of i

☐ Because: $var(u_i) = (A)_{ii}\,\sigma_u^2 = (1+F_i)\sigma_u^2$

$\Rightarrow (A)_{ii} = 1+F_i$

☐ Inbreeding is related to the probability of two alleles at one given locus in a given animal i are identical by descent.

OHP Picture 3



- ☐ Inbreeding seams to be related to a higher degree of similarity at the genotype level, because inbreeding can only occur at homozygous loci.
- ☐ var(u_i) of breeding value u_i is increased with a higher level of inbreeding (F_i)

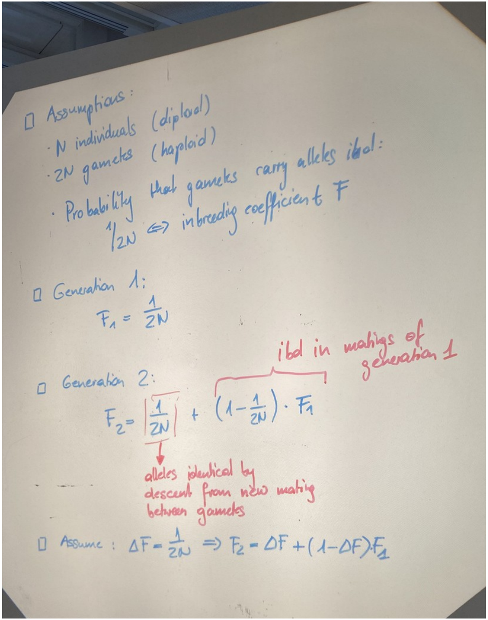
Solution: How does inbreeding gets introduced in a population?

Base Population (idealised population) ($N \rightarrow \infty$ infinite population size) (no selection, no migration, no drift)

Isolation within lines, i.e., animals or gametes do not mix between lines.

Examples: OB dairy cows 8 bulls migrated to N-America

OHP Picture 4



☐ Assumptions:

- N individuals (diploid)
- 2N gametes (haploid)
- Probability that gametes carry alleles ibd:
  $1/2N \Leftrightarrow$ inbreeding coefficient F

☐ Generation 1:

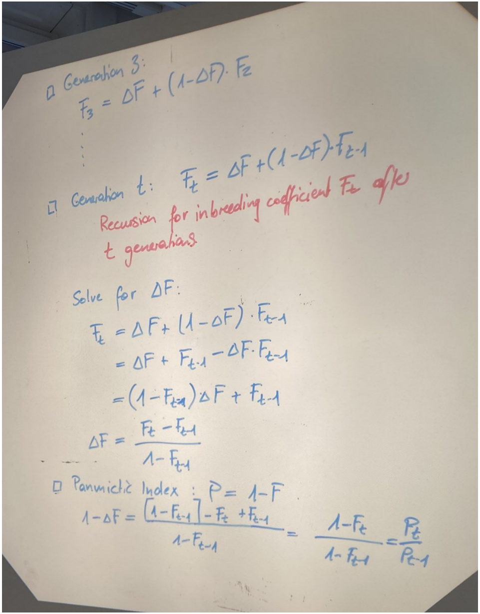
$$F_1 = \frac{1}{2N}$$

☐ Generation 2:

$$F_2 = \underbrace{\boxed{\frac{1}{2N}}}_{\text{alleles identical by descent from new mating between gametes}} + \overbrace{\left(1-\frac{1}{2N}\right)\cdot F_1}^{\text{ibd in matings of generation 1}}$$

☐ Assume: $\Delta F = \frac{1}{2N} \Rightarrow F_2 = \Delta F + (1-\Delta F)\cdot F_1$

OHP Picture 5



☐ Generation 3:

$$F_3 = \Delta F + (1-\Delta F)\cdot F_2$$

$\vdots$

☐ Generation t: $F_t = \Delta F + (1-\Delta F)\cdot F_{t-1}$

Recursion for inbreeding coefficient F_t after t generations

Solve for ΔF:

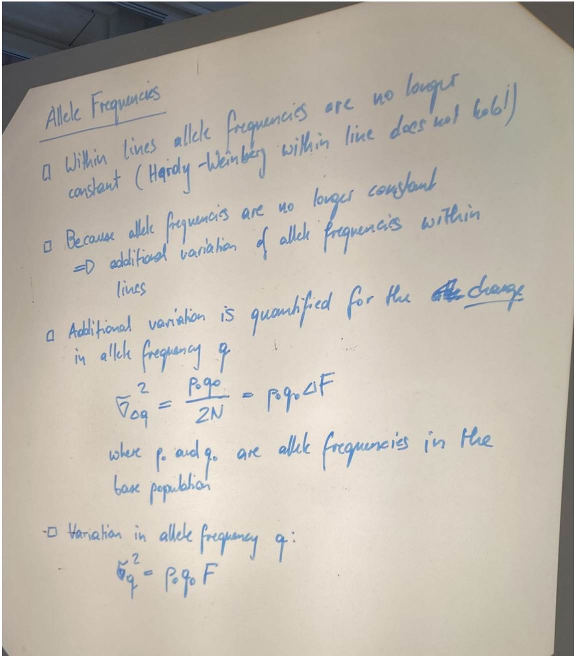
$$\begin{aligned} F_t &= \Delta F + (1-\Delta F)\cdot F_{t-1} \\ &= \Delta F + F_{t-1} - \Delta F\cdot F_{t-1} \\ &= (1-F_{t-1})\Delta F + F_{t-1} \end{aligned}$$

$$\Delta F = \frac{F_t - F_{t-1}}{1-F_{t-1}}$$

☐ Panmictic Index : $P = 1-F$

$$1-\Delta F = \frac{[1-F_{t-1}] - F_t + F_{t-1}}{1-F_{t-1}} = \frac{1-F_t}{1-F_{t-1}} = \frac{P_t}{P_{t-1}}$$

OHP Picture 6



Allele Frequencies

☐ Within lines allele frequencies are no longer constant (Hardy-Weinberg within line does not hold!)

☐ Because allele frequencies are no longer constant
=> additional variation of allele frequencies within lines

☐ Additional variation is quantified for the ~~the~~ change in allele frequency q

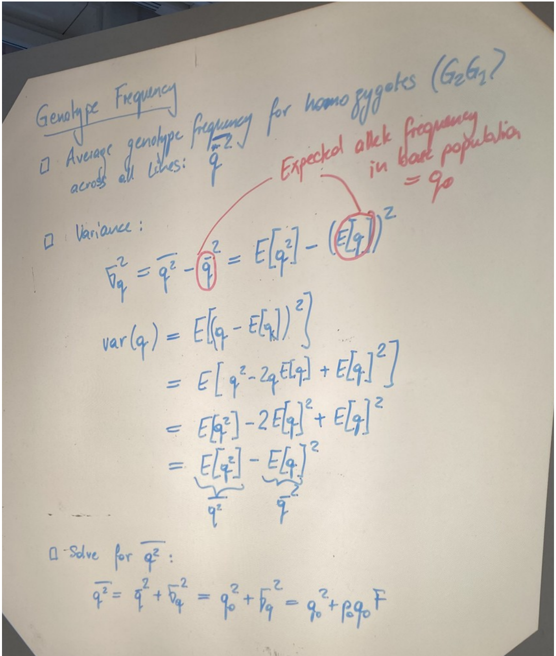
$$\sigma^2_{\Delta q} = \frac{p_0 q_0}{2N} = p_0 q_0 \Delta F$$

where p_0 and q_0 are allele frequencies in the base population

☐ Variation in allele frequency q:

$$\sigma^2_q = p_0 q_0 F$$

OHP Picture 7



Genotype Frequency

☐ Average genotype frequency for homozygotes (G_2G_2)? across all lines: $\overline{q^2}$

Expected allele frequency in base population $= q_0$

☐ Variance:

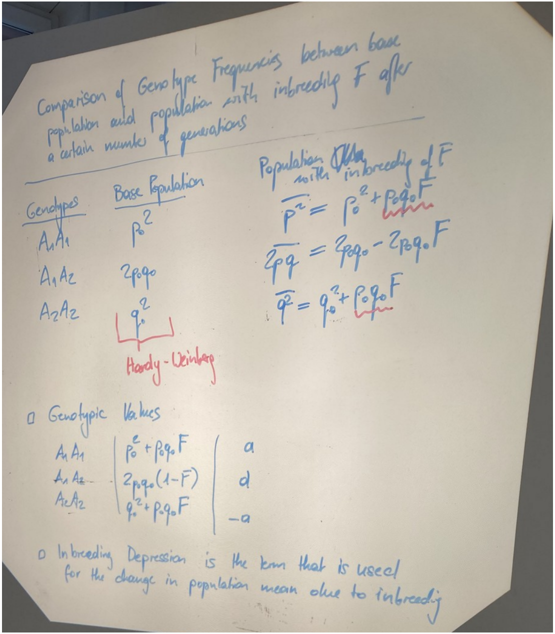
$$\sigma_q^2 = \overline{q^2} - \boxed{\bar{q}}^2 = E[q^2] - \left(\boxed{E[q]}\right)^2$$

$$\begin{aligned} \mathrm{var}(q) &= E\left[(q - E[q]))^2\right] \\ &= E\left[q^2 - 2qE[q] + E[q]^2\right] \\ &= E[q^2] - 2E[q]^2 + E[q]^2 \\ &= \underbrace{E[q^2]}_{\overline{q^2}} - \underbrace{E[q]^2}_{\bar{q}^2} \end{aligned}$$

☐ Solve for $\overline{q^2}$:

$$\overline{q^2} = \bar{q}^2 + \sigma_q^2 = q_0^2 + \sigma_q^2 = q_0^2 + p_0 q_0 F$$

OHP Picture 8



Comparison of Genotype Frequencies between base population and population with inbreeding F after a certain number of generations

Genotypes	Base Population	Population with inbreeding of F
A_1A_1	p_0^2	$\overline{p^2} = p_0^2 + p_0q_0F$
A_1A_2	$2p_0q_0$	$\overline{2pq} = 2p_0q_0 - 2p_0q_0F$
A_2A_2	q_0^2	$\overline{q^2} = q_0^2 + p_0q_0F$

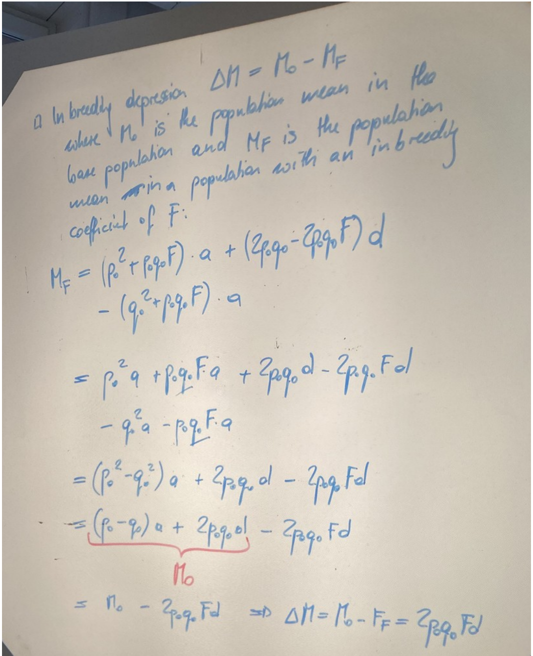
Hardy-Weinberg

- ☐ Genotypic Values

A_1A_1	$p_0^2 + p_0q_0F$	a
A_1A_2	$2p_0q_0(1-F)$	d
A_2A_2	$q_0^2 + p_0q_0F$	$-a$

- ☐ Inbreeding Depression is the term that is used for the change in population mean due to inbreeding

OHP Picture 9



□ Inbreeding depression $\Delta M = M_0 - M_F$ where M_0 is the population mean in the base population and M_F is the population mean in a population with an inbreeding coefficient of F:

$$M_F = (p_0^2 + p_0 q_0 F) \cdot a + (2p_0q_0 - 2p_0q_0F)\, d - (q_0^2 + p_0q_0F) \cdot a$$

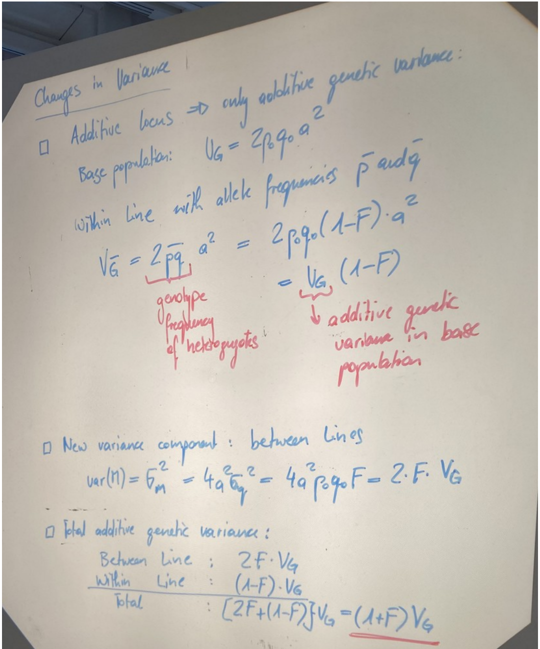
$$= p_0^2 a + p_0q_0Fa + 2p_0q_0 d - 2p_0q_0Fd - q_0^2 a - p_0q_0F a$$

$$= (p_0^2 - q_0^2)\, a + 2p_0q_0 d - 2p_0q_0Fd$$

$$= \underbrace{(p_0 - q_0)\, a + 2p_0q_0 d}_{M_0} - 2p_0q_0Fd$$

$$= M_0 - 2p_0q_0Fd \Rightarrow \Delta M = M_0 - F_F = 2p_0q_0Fd$$

OHP Picture 10



Changes in Variance

☐ Additive locus ⇒ only additive genetic variance:

Base population: $V_G = 2p_0q_0a^2$

Within line with allele frequencies $\bar{p}$ and $\bar{q}$

$$V_{\bar{G}} = \underbrace{2\overline{pq}}_{\text{genotype frequency of heterozygotes}}\, a^2 = 2p_0q_0(1-F)\cdot a^2$$

$$= \underbrace{V_G}_{\text{additive genetic variance in base population}}(1-F)$$

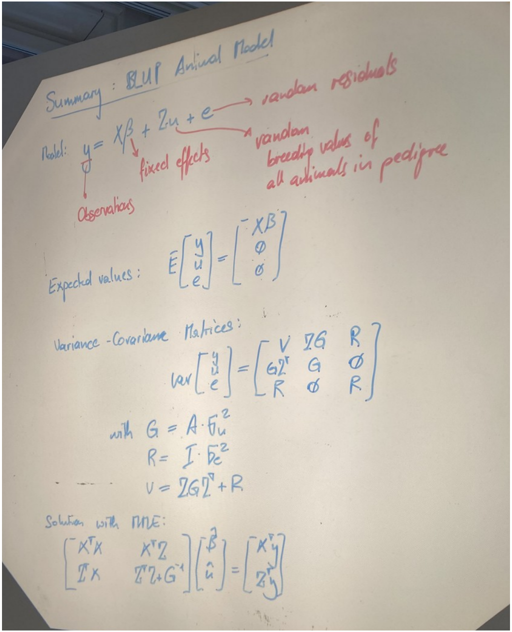
☐ New variance component: between lines

$$var(M) = \sigma_M^2 = 4a^2\sigma_q^2 = 4a^2p_0q_0F = 2\cdot F\cdot V_G$$

☐ Total additive genetic variance:

Between line : $2F\cdot V_G$
Within line : $(1-F)\cdot V_G$
Total : $[2F+(1-F)]V_G = \underline{(1+F)V_G}$

OHP Picture 11



Summary : BLUP Animal Model

Model: $y = X\beta + Zu + e$

- y → Observations
- $X\beta$ → fixed effects
- e → random residuals
- Zu → random breeding values of all animals in pedigree

Expected values: $E\begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} X\beta \\ 0 \\ 0 \end{bmatrix}$

Variance-Covariance Matrices:

$$\mathrm{var}\begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} V & ZG & R \\ GZ^T & G & 0 \\ R & 0 & R \end{bmatrix}$$

with $G = A \cdot \sigma_u^2$

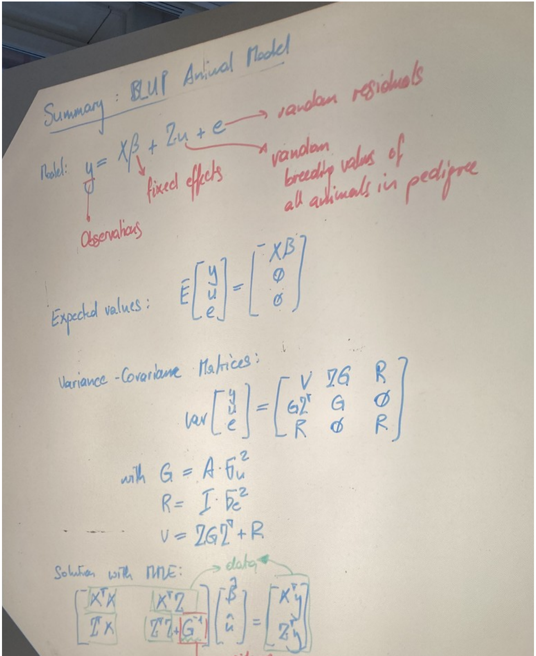
$R = I \cdot \sigma_e^2$

$V = ZGZ^T + R$

Solution with MME:

$$\begin{bmatrix} X^TX & X^TZ \\ Z^TX & Z^TZ + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^Ty \\ Z^Ty \end{bmatrix}$$

OHP Picture 12



Summary : BLUP Animal Model

Model: $y = X\beta + Zu + e$

y → Observations

$X\beta$ → fixed effects

Zu → random breeding values of all animals in pedigree

e → random residuals

Expected values: $E\begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} X\beta \\ \emptyset \\ \emptyset \end{bmatrix}$

Variance-Covariance Matrices:

$$var\begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} V & ZG & R \\ GZ^T & G & \emptyset \\ R & \emptyset & R \end{bmatrix}$$

with $G = A \cdot \sigma_u^2$

$R = I \cdot \sigma_e^2$

$V = ZGZ^T + R$

Solution with MME:

data

$$\begin{bmatrix} X^TX & X^TZ \\ Z^TX & Z^TZ + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^Ty \\ Z^Ty \end{bmatrix}$$