OHP Picture 1

Recap: Fixed Linear Effects Model

$$y_{ij} = \overbrace{\mu + herd_j}^{\text{unknown}} + e_{ij}$$

e_{ij} → random residual → unknown

μ → intercept

j → known

$herd_j$ → effect of $herd_j$ on weaning weight

y_{ij} → $\underbrace{\text{Weaning weight}}_{\text{known from data}}$ of animal i in $herd_j$

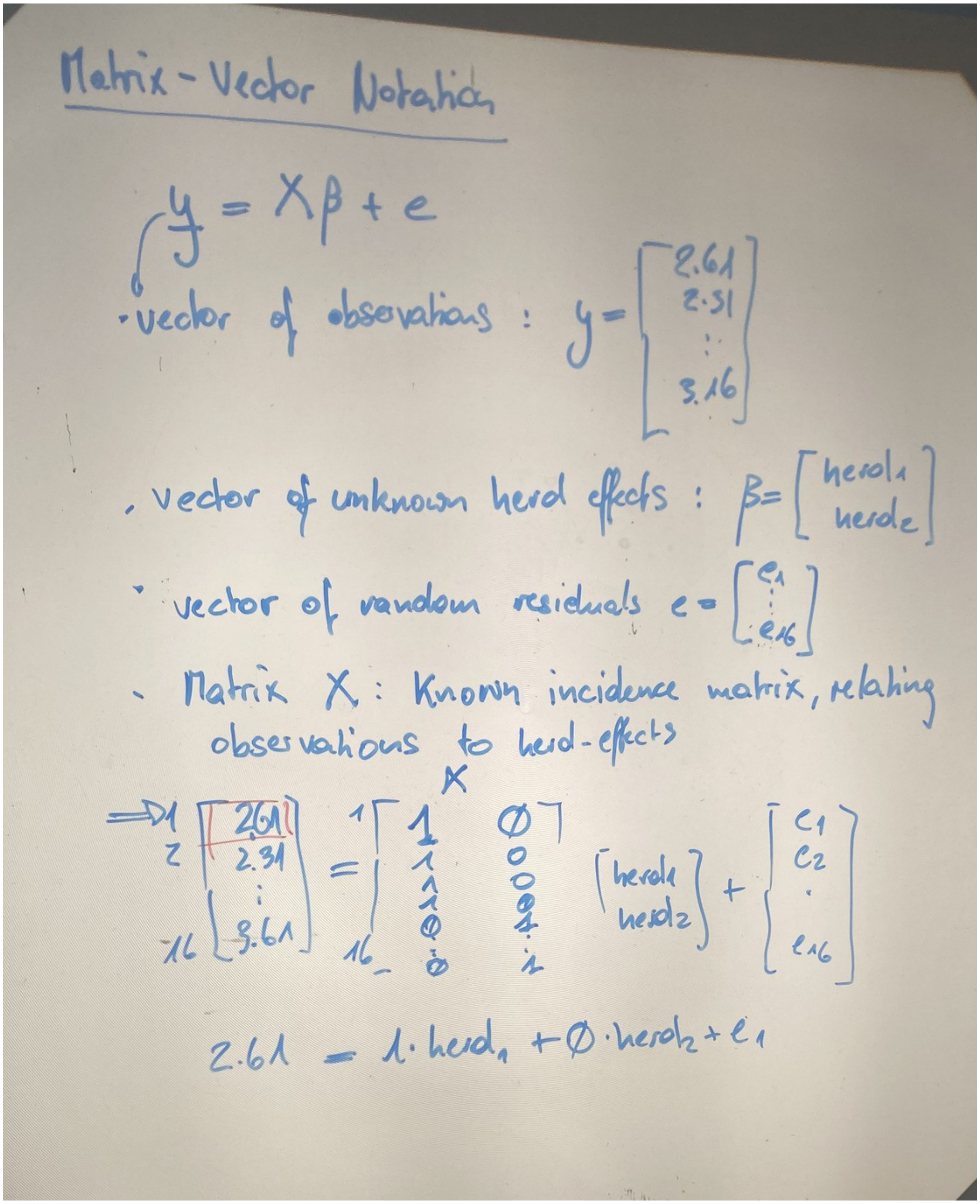
Goal: What are the effects of different herds on response variable (y), in our example weaning weight.

Modelling Procedure: Step 1: Info from the dataset into the model

$$\begin{cases} y_{12,1} = \mu + herd_1 + e_{12,1} \Leftrightarrow 2.61 = \mu + herd_1 + e_{12,1} \\ \vdots \\ y_{27,2} = \mu + herd_2 + e_{27,2} \Leftrightarrow 3.61 = \mu + herd_2 + e_{27,2} \end{cases}$$

→ least squares to solve for effects of μ, $herd_1$, $herd_2$

OHP Picture 2



OHP Picture 3

Regression of weaning weight on breast circumference

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

$$y = \begin{bmatrix} 2.61 \\ 2.51 \\ \vdots \end{bmatrix} \; ; \; \beta = \begin{bmatrix} \text{intercept} \\ \text{regression coefficient} \end{bmatrix}$$

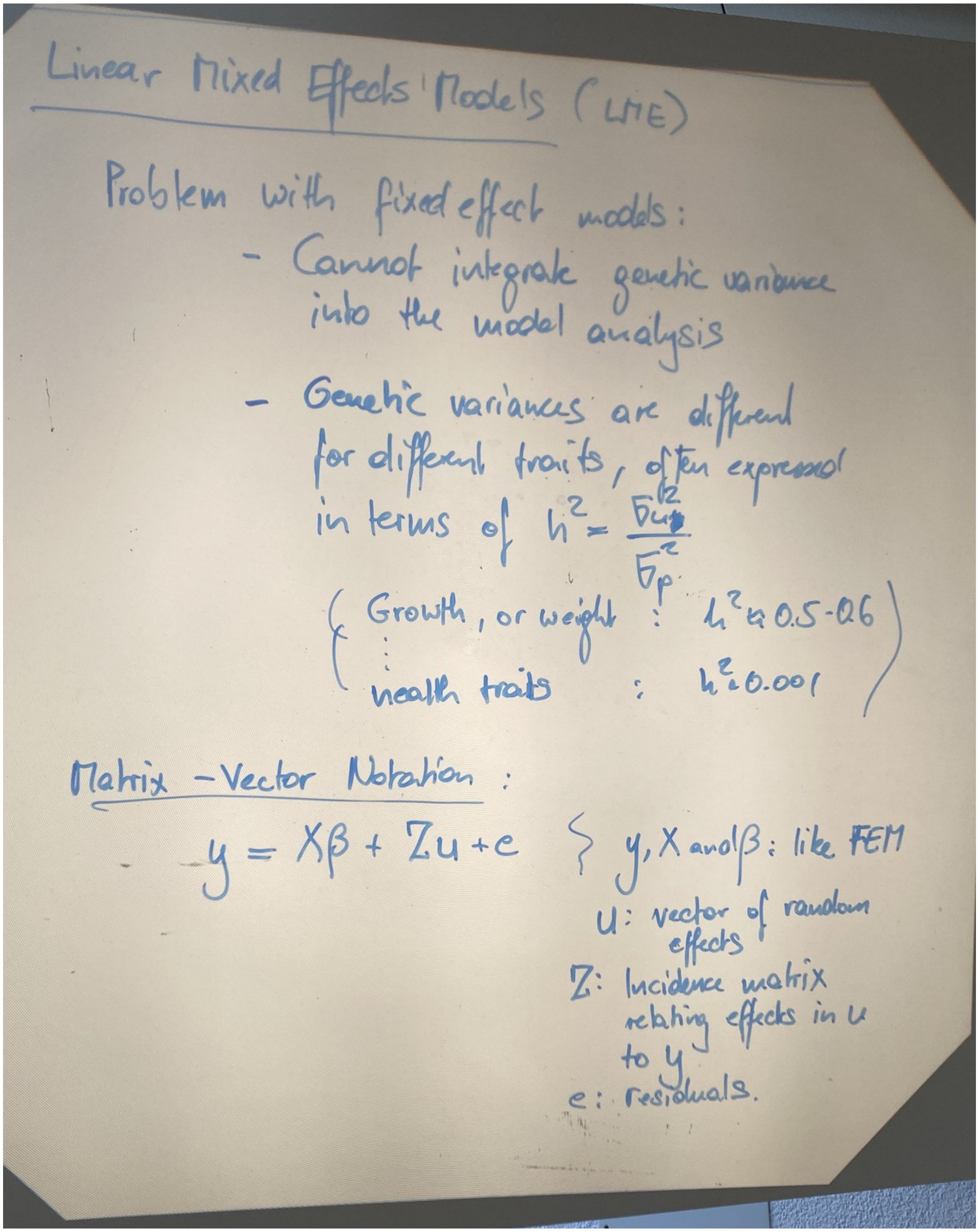
$$e = \begin{bmatrix} e_1 \\ \vdots \\ e_{10} \end{bmatrix} \; , \; X = \begin{bmatrix} 1 & 1.62 \\ 1 & 1.96 \\ \vdots & \vdots \\ 1 & \vdots \end{bmatrix}$$

Goal get estimates for unknown β using least squares.

$$\hat{\beta} = (X^T X)^{-1} \cdot X^T y \; ; \; \hat{se}_r = \sqrt{\frac{1}{n-2} \sum_{i=1}^{n} r_i^2}$$

Verify with R: lm()

OHP Picture 4



Linear Mixed Effects Models (LME)

Problem with fixed effect models:

- Cannot integrate genetic variance into the model analysis
- Genetic variances are different for different traits, often expressed in terms of $h^2 = \frac{\sigma_u^2}{\sigma_p^2}$

$$\left\{ \begin{array}{ll} \text{Growth, or weight} & : \quad h^2 \approx 0.5 - 0.6 \\ \vdots & \\ \text{health traits} & : \quad h^2 \approx 0.001 \end{array} \right)$$

Matrix-Vector Notation:

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

y, X and β: like FEM

u: vector of random effects

Z: Incidence matrix relating effects in u to y

e: residuals.

OHP Picture 5

For a LME, also the definition of the expected values and the variance-covariance matrices are important.

- Expected values:

$$E(\underline{u}) = \underline{0} = E\begin{bmatrix} u_1 \\ u_2 \\ \vdots \\ u_K \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}$$

$$E(\underline{e}) = E\begin{bmatrix} e_1 \\ e_2 \\ \vdots \\ e_N \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} = \underline{0}$$

$$E(y) = E[X\beta + Zu + e] = E[X\beta] + E[Zu] + E[e]$$

$$= E[X\beta] + Z \cdot \underbrace{E[\underline{u}]}_{=0} + \underbrace{E[e]}_{0}$$

$$= X\,E[\beta] = X\beta$$

Variances: $\underbrace{var(\underline{u})}_{\text{Variance-covariance Matrix}} = G = \begin{bmatrix} var(u_1) & cov(u_1,u_2) & \cdots \\ cov(u_2,u_1) & var(u_2) & \cdots \end{bmatrix}$

$$var(\underline{e}) = R$$

Covariance between u and e:

$$cov(u, e^T) = \begin{bmatrix} cov(u_1,e_1) & cov(u_1,e_2) & \cdots \\ cov(u_2,e_1) & cov(u_2,e_2) & \cdots \end{bmatrix}$$

OHP Picture 6

Covariance between u and e:

$$\mathrm{cov}(u, e^T) = \begin{bmatrix} \mathrm{cov}(u_1, e_1) & \mathrm{cov}(u_1, e_2) & \cdots \\ \mathrm{cov}(u_2, e_1) & \mathrm{cov}(u_2, e_2) & \cdots \\ \vdots & & \end{bmatrix} = 0$$

Assume no covariance between genetic effects and environment (no G×E interactions)

$$\mathrm{cov}(y, u^T) = \mathrm{cov}(X\beta + Zu + e, u^T)$$

$$= \underbrace{\mathrm{cov}(\underbrace{X\beta}_{\text{fix}}, \underbrace{u^T}_{\text{random}})}_{=0} + \mathrm{cov}(Zu, u^T) + \overbrace{\mathrm{cov}(e, u^T)}^{\mathrm{cov}(u, e^T) = 0}$$

$$= \mathrm{cov}(Zu, u^T) = Z\,\mathrm{cov}(u, u^T)$$

$$= Z \cdot \mathrm{var}(u) = ZG$$

$$\mathrm{var}(y) = \mathrm{var}(X\beta + Zu + e) = \overbrace{\mathrm{var}(X\beta)}^{=0} + \mathrm{var}(Zu) + \mathrm{var}(e)$$

$$+ \underbrace{2\,\mathrm{cov}(X\beta, u^T Z^T)}_{=0} + 2\underbrace{\mathrm{cov}(X\beta, e^T)}_{=0} + 2\,\mathrm{cov}\underbrace{(Zu, e^T)}_{=0}$$

$$= \mathrm{var}(Zu) + \mathrm{var}(e)$$

$$= Z \cdot \mathrm{var}(u) \cdot Z^T + R = Z \cdot G \cdot Z^T + R = V$$

Unknown effects for which we want to compute estimates:

- fixed effects: β
- random effects: u (predictions)

OHP Picture 7

Unknown effects for which we want to compute estimates:

- fixed effects: β
- random effects: u (predictions)

• Predictions of random effects are based on conditional expectation:

$$\hat{\underline{u}} = E(\underline{u} \mid \underline{y}) = Cov(\underline{u}, \underline{y}^T) \cdot var(\underline{y})^{-1} \cdot (\underline{y} - X\hat{\beta})$$

$$= \underline{Z} \cdot G \, V^{-1} (\underline{y} - X\beta) \rightarrow \text{unknown}$$

Remember: Own performance record, we defined

$$\hat{u} = E(u \mid y) = \frac{cov(u,y)}{var(y)} \cdot (y - \mu)$$

• For fixed effects: Least Squares Estimate is used:

$$\hat{\beta} = (X^T V^{-1} X)^{-} X^T V^{-1} y$$

$\rightarrow$ Dimension $\Downarrow$ $10^7 \times 10^7$

Mixed Model Equations:

$$\begin{bmatrix} X^T R^{-1} X & X^T R^{-1} Z \\ Z^T R^{-1} X & Z^T R^{-1} Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^T R^{-1} y \\ Z^T R^{-1} y \end{bmatrix}$$

OHP Picture 8

Mixed Model Equations:

$$\begin{bmatrix} X^T R^{-1} X & X^T R^{-1} Z \\ Z^T R^{-1} X & Z^T R^{-1} Z + G^{-1} \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^T R^{-1} y \\ Z^T R^{-1} y \end{bmatrix}$$

solve for $\hat{\beta}$ and $\hat{u}$ $\Rightarrow$ equivalent to above solutions

In MME R^{-1} a much simpler structure. We assume residuals are uncorrelated, i.e. $cov(e_i, e_j) = 0$ and $var(e_i) = \sigma_e^2 \Rightarrow R = \underbrace{I}_{\text{Identity matrix}} \cdot \sigma_e^2$

$$\Rightarrow R^{-1} = I \cdot \sigma_e^{-2}$$

$$\Rightarrow \begin{bmatrix} \boxed{X^T X} & X^T Z \\ Z^T X & Z^T Z + G^{-1} \cdot \sigma_e^2 \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X^T y \\ Z^T y \end{bmatrix}$$

Obtained from data directly

Sire Model: is a LME with sire effects as random model terms.

$$y = X\beta + Zs + e$$

sire effects, genetic contribution of a sire to an observation in an offspring (introduced in dairy cattle)

OHP Picture 9

Insert information from data into model:

y, X, β – fixed effect model

$$\underbrace{\begin{bmatrix} 2.61 \\ 3.31 \\ \vdots \\ \vdots \end{bmatrix}}_{y} = \underbrace{\begin{bmatrix} 1 & 0 \\ 1 & 0 \\ \vdots & \vdots \\ 0 & 1 \end{bmatrix}}_{X} \underbrace{\begin{bmatrix} herd_1 \\ herd_2 \end{bmatrix}}_{\beta} + \underbrace{\begin{bmatrix} 1 & 0 & 0 \\ \vdots & \vdots & \vdots \\ 0 & 1 & 0 \\ \vdots & \vdots & \vdots \\ 0 & 0 & 1 \end{bmatrix}}_{Z} \underbrace{\begin{bmatrix} s_1 \\ s_2 \\ s_3 \end{bmatrix}}_{s} + \underbrace{\begin{bmatrix} e_1 \\ \vdots \\ e_{16} \end{bmatrix}}_{e}$$

$E[e] = 0$; $E[s] = 0$; $E(y) = X\beta$

$var(e) = R = I \cdot \sigma_e^2$; $var(s) = \begin{bmatrix} var(s_1) & cov(s_1,s_2) & cov(s_1,s_3) \\ \vdots & & \\ \vdots & & \end{bmatrix}$

Assume sires 1, 2 and 3 are unrelated, i.e they do not share any common ancestors

$\Rightarrow cov(s_1, s_2) = cov(s_1, s_3) = cov(s_2, s_3) = 0$

$\Rightarrow G = var(s) = I \cdot \sigma_s^2$

Find solutions for estimates $\hat{\beta}$ and predictions $\hat{s}$ using Mixed Model Equations:

$$\begin{bmatrix} X^T X & X^T Z \\ Z^T X & Z^T Z + I \cdot \sigma_e^2 / \sigma_s^2 \end{bmatrix} \begin{bmatrix} \hat{\beta} \\ \hat{s} \end{bmatrix} = \begin{bmatrix} X^T y \\ Z^T y \end{bmatrix}$$