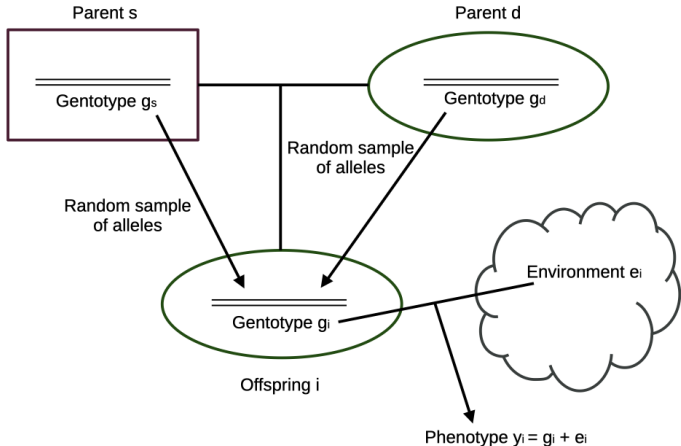


# Applications of Linear Mixed Effects Models

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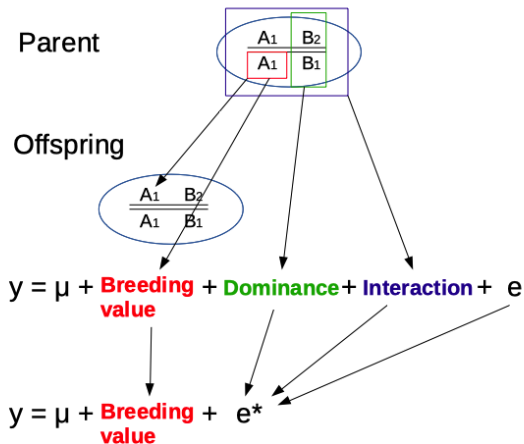
# Background

- ▶ Parents pass a random sample of alleles to offspring
- ▶ Selection of parents on phenotypes inefficient



## Selection Criterion

- ▶ Quantify value of alleles passed from parent to offspring
- ▶ Requires decomposition of effect of genotype on phenotype



# Model Based on Decomposition of Genotype

- ▶ Further transformation of genotype decomposition

$$y = \mu + \text{Breeding value} + \text{Dominance} + \text{Interaction} + e$$

$$y = \mu + \text{Breeding value} + e^*$$

$$y = \underbrace{Xb}_{\text{Intercept}} + Zu + e$$

Intercept  
Fixed and known part  
of environment

Non-additive gene effects  
Random unknown part  
of environment

# Statistical Model

- ▶ Linear Mixed Effects Model

$$y = Xb + Zu + e$$

- ▶ with vectors

- ▶  $y$  of length  $n$  with observations

- ▶  $b$  of length  $p$  with fixed effects

- ▶  $u$  of length  $q$  with random breeding values

- ▶  $e$  of length  $n$  with random residuals

- ▶ with design matrices  $X$  and  $Z$

## Assumptions

Expected values and variance-covariance matrices of all random components

$$E \begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} Xb \\ 0 \\ 0 \end{bmatrix}$$

$$\text{var} \begin{bmatrix} y \\ u \\ e \end{bmatrix} = \begin{bmatrix} V & ZU & R \\ UZ^T & U & 0 \\ R & 0 & R \end{bmatrix}$$

with

- ▶  $R = I * \sigma_e^2$
- ▶  $U = A * \sigma_u^2$ , where  $A$  is a genetic relationship matrix
- ▶  $V = ZUZ^T + R$

# Inference

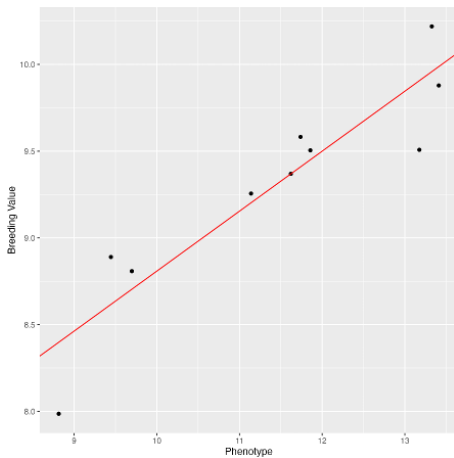
- ▶ Estimates of unknown fixed effects ( $b$ )
- ▶ Predictions of  $u$

Analogous to fixed effects model, estimates  $\hat{b}$  are given by

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

# Prediction of Breeding Values

Assume, breeding values ( $u$ ) and phenotypes ( $y$ ) can be observed





## Prediction of Breeding Values II

- ▶ For new animal  $i$  with phenotypic observation  $y_i$
- ▶ Breeding value  $u_i$  can be predicted based on regression line, as

$$\widehat{u}_i = \mu_u + b * (y_i - \mu_y)$$

## Generalisation

- ▶ Assuming multi-variate normal distributions for  $y$ ,  $u$  and  $e$
- ▶ For animal  $i$

$$\hat{u}_i = E(u_i|y_i) = E(u_i) + \frac{\text{cov}(u_i, y_i)}{\text{var}(y_i)} * (y_i - E(y_i))$$

- ▶ For a group of animals

$$\hat{u} = E(u|y) = E(u) + \text{cov}(u, y^T) \cdot \text{var}(y)^{-1} \cdot (y - E(y))$$

$$\hat{u} = UZ^T \cdot V^{-1} \cdot (y - Xb)$$

## Simplified Solution: Mixed Model Equations

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

with  $R = I * \sigma_e^2$

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

with  $\lambda = \sigma_e^2 / \sigma_u^2$

# Examples

- ▶ Sire model
- ▶ Animal model
- ▶ Genomic BLUP