Linear Mixed-Effects Models

The Linear Mixed-Effects Model

- $\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e}$
- $\boldsymbol{X}$ is an $n \times p$ design matrix of known constants
- $\boldsymbol{\beta} \in \mathbb{R}^p$ is an unknown parameter vector
- $\boldsymbol{Z}$ is an $n \times q$ matrix of known constants
- $\boldsymbol{u}$ is a $q \times 1$ random vector
- $\boldsymbol{e}$ is an $n \times 1$ vector of random errors

The Linear Mixed-Effects Model

- $\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e}$

- The elements of $\boldsymbol{\beta}$ are considered to be non-random and are called "fixed effects."

- The elements of $\boldsymbol{u}$ are random variables and are called "random effects."

- The elements of the error vector $\boldsymbol{e}$ are always considered to be random variables.

- Because the model includes both fixed and random effects (in addition to the random errors), it is called a “mixed-effects” model or, more simply, a “mixed” model.

- The model is called a “linear” mixed-effects model because (as we will soon see)

$$E(\boldsymbol{y}|\boldsymbol{u}) = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{Z}\boldsymbol{u},$$

  a linear function of fixed and random effects.

We assume that

$$E(\boldsymbol{e}) = \mathbf{0} \qquad \mathrm{Var}(\boldsymbol{e}) = \boldsymbol{R}$$

$$E(\boldsymbol{u}) = \mathbf{0} \qquad \mathrm{Var}(\boldsymbol{u}) = \boldsymbol{G}$$

$$\mathrm{Cov}(\boldsymbol{e},\ \boldsymbol{u}) = \mathbf{0}.$$

It follows that

$$
\begin{aligned}
\boldsymbol{E}(\boldsymbol{y}) &= \boldsymbol{E}(\boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{e}) \\
&= \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{Z}\boldsymbol{E}(\boldsymbol{u}) + \boldsymbol{E}(\boldsymbol{e}) \\
&= \boldsymbol{X}\boldsymbol{\beta}
\end{aligned}
$$

$$
\begin{aligned}
\mathrm{Var}(\boldsymbol{y}) &= \mathrm{Var}(\boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{e}) \\
&= \mathrm{Var}(\boldsymbol{Z}\boldsymbol{u} + \boldsymbol{e}) \\
&= \mathrm{Var}(\boldsymbol{Z}\boldsymbol{u}) + \mathrm{Var}(\boldsymbol{e}) \\
&= \boldsymbol{Z}\mathrm{Var}(\boldsymbol{u})\boldsymbol{Z}' + \boldsymbol{R} \\
&= \boldsymbol{Z}\boldsymbol{G}\boldsymbol{Z}' + \boldsymbol{R} \equiv \boldsymbol{\Sigma}.
\end{aligned}
$$

We usually consider the special case in which

$$\begin{bmatrix} \boldsymbol{u} \\ \boldsymbol{e} \end{bmatrix} \sim N\left(\begin{bmatrix} \boldsymbol{0} \\ \boldsymbol{0} \end{bmatrix}, \begin{bmatrix} \boldsymbol{G} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{R} \end{bmatrix} \right)$$

$$\implies \boldsymbol{y} \sim N(\boldsymbol{X\beta}, \boldsymbol{ZGZ}' + \boldsymbol{R}).$$

The conditional moments, given the random effects, are

$$\boldsymbol{E}(\boldsymbol{y}|\boldsymbol{u}) = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{Z}\boldsymbol{u}$$

$$\mathrm{Var}(\boldsymbol{y}|\boldsymbol{u}) = \boldsymbol{R}.$$

Example 1

Suppose a study was conducted to compare two plant genotypes (genotype 1 and genotype 2). Suppose 10 seeds (5 of genotype 1 and 5 of genotype 2) were planted in a total of 4 pots. Suppose 3 genotype 1 seeds were planted in one pot, and the other 2 genotype 1 seeds were planted in another pot. Suppose the same planting strategy was used when planting genotype 2 seeds in the other two pots. The seeds germinated and emerged from the soil as seedlings. After a four-week growing period, each seedling was dried and weighed. Let y_{ijk} denote the weight for genotype i, pot j, seedling k. Provide a linear mixed-effects model for the dry-weight data. Determine $\boldsymbol{y}$, $\boldsymbol{X}$, $\boldsymbol{\beta}$, $\boldsymbol{Z}$, $\boldsymbol{u}$, $\boldsymbol{G}$, $\boldsymbol{R}$, and $\mathrm{Var}(\boldsymbol{y})$.

Consider the model

$$y_{ijk} = \mu + \gamma_i + p_{ij} + e_{ijk}$$

$$p_{11}, p_{12}, p_{21}, p_{22} \overset{i.i.d.}{\sim} N(0, \sigma_p^2)$$

independent of the e_{ijk} terms, which are assumed to be iid $N(0, \sigma_e^2)$.

This model can be written in the form

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e}, \text{ where}$$

$$
\boldsymbol{y} = \begin{bmatrix} y_{111} \\ y_{112} \\ y_{113} \\ y_{121} \\ y_{122} \\ y_{211} \\ y_{212} \\ y_{213} \\ y_{221} \\ y_{222} \end{bmatrix}, \quad \boldsymbol{X} = \begin{bmatrix} 1 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 1 & 0 \\ 1 & 0 & 1 \\ 1 & 0 & 1 \\ 1 & 0 & 1 \\ 1 & 0 & 1 \\ 1 & 0 & 1 \end{bmatrix}, \quad \boldsymbol{\beta} = \begin{bmatrix} \mu \\ \gamma_1 \\ \gamma_2 \end{bmatrix},
$$

$$\boldsymbol{Z} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{bmatrix}, \ \boldsymbol{u} = \begin{bmatrix} p_{11} \\ p_{12} \\ p_{21} \\ p_{22} \end{bmatrix}, \ \boldsymbol{e} = \begin{bmatrix} e_{111} \\ e_{112} \\ e_{113} \\ e_{121} \\ e_{122} \\ e_{211} \\ e_{212} \\ e_{213} \\ e_{221} \\ e_{222} \end{bmatrix}.$$

$$\boldsymbol{G} = \mathrm{Var}(\boldsymbol{u}) = \mathrm{Var}([p_{11}, p_{12}, p_{21}, p_{22}]') = \sigma_p^2 \boldsymbol{I}_{4\times 4}$$

$$\boldsymbol{R} = \mathrm{Var}(\boldsymbol{e}) = \sigma_e^2 \boldsymbol{I}_{10\times 10}$$

$$\mathrm{Var}(\boldsymbol{y}) = \boldsymbol{Z}\boldsymbol{G}\boldsymbol{Z}' + \boldsymbol{R} = \boldsymbol{Z}\sigma_p^2 \boldsymbol{I}\boldsymbol{Z}' + \sigma_e^2 \boldsymbol{I} = \sigma_p^2 \boldsymbol{Z}\boldsymbol{Z}' + \sigma_e^2 \boldsymbol{I}.$$

$$\boldsymbol{ZZ'} = \begin{bmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \end{bmatrix}$$

Thus, $\mathrm{Var}(\boldsymbol{y}) = \sigma_p^2 \boldsymbol{Z}\boldsymbol{Z}' + \sigma_e^2 \boldsymbol{I}$ is a block diagonal matrix.

The first block is

$$\mathrm{Var}\begin{bmatrix} y_{111} \\ y_{112} \\ y_{113} \end{bmatrix} = \begin{bmatrix} \sigma_p^2 + \sigma_e^2 & \sigma_p^2 & \sigma_p^2 \\ \sigma_p^2 & \sigma_p^2 + \sigma_e^2 & \sigma_p^2 \\ \sigma_p^2 & \sigma_p^2 & \sigma_p^2 + \sigma_e^2 \end{bmatrix}.$$

Note that

$$
\begin{aligned}
\mathrm{Var}(y_{ijk}) &= \sigma_p^2 + \sigma_e^2 \qquad \forall\ i, j, k. \\
\mathrm{Cov}(y_{ijk},\ y_{ijk^*}) &= \sigma_p^2 \qquad \forall\ i, j, \text{ and } k \neq k^*. \\
\mathrm{Cov}(y_{ijk},\ y_{i^*j^*k^*}) &= 0 \qquad \text{if } i \neq i^* \text{ or } j \neq j^*.
\end{aligned}
$$

Any two observations from the same pot have covariance σ_p^2.

Any two observations from different pots are uncorrelated.

- Note that $\mathrm{Var}(\boldsymbol{y})$ may be written as $\sigma_e^2\boldsymbol{V}$ where $\boldsymbol{V}$ is a block diagonal matrix with blocks of the form

$$\begin{bmatrix} 1+\sigma_p^2/\sigma_e^2 & \sigma_p^2/\sigma_e^2 & . \quad . \quad . & \sigma_p^2/\sigma_e^2 \\ \sigma_p^2/\sigma_e^2 & 1+\sigma_p^2/\sigma_e^2 & . \quad . \quad . & \sigma_p^2/\sigma_e^2 \\ . & . & . \qquad\qquad & . \\ . & . & . & . \\ . & . & \qquad\qquad . & . \\ \sigma_p^2/\sigma_e^2 & \sigma_p^2/\sigma_e^2 & . \quad . \quad . & 1+\sigma_p^2/\sigma_e^2 \end{bmatrix}$$

- Thus, if σ_p^2/σ_e^2 were known, we would have the Aitken Model.

$$\boldsymbol{y} = \boldsymbol{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}, \text{ where } \boldsymbol{\varepsilon} = \boldsymbol{Z}\boldsymbol{u} + \boldsymbol{e} \sim N(\boldsymbol{0},\ \sigma^2\boldsymbol{V}),\ \sigma^2 \equiv \sigma_e^2.$$

- Thus, if σ_p^2/σ_e^2 were known, we would use GLS to estimate any estimable $\boldsymbol{C}\boldsymbol{\beta}$ by $\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\text{GLS}} = \boldsymbol{C}(\boldsymbol{X}'\boldsymbol{V}^{-1}\boldsymbol{X})^{-}\boldsymbol{X}'\boldsymbol{V}^{-1}\boldsymbol{y}$.

- However, we seldom know σ_p^2/σ_e^2 or, more generally, $\boldsymbol{\Sigma}$ or $\boldsymbol{V}$.

- For the general problem where $\text{Var}(\boldsymbol{y}) = \boldsymbol{\Sigma}$ is an unknown positive definite matrix, we can rewrite $\boldsymbol{\Sigma}$ as $\sigma^2\boldsymbol{V}$, where σ^2 is an unknown positive variance and $\boldsymbol{V}$ is an unknown positive definite matrix.

- As in our simple example, each entry of $\boldsymbol{V}$ is usually assumed to be a known function of few unknown parameters.

- Thus, our strategy for estimating an estimable $\boldsymbol{C}\boldsymbol{\beta}$ involves estimating the unknown parameters in $\boldsymbol{V}$ to obtain

$$\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\widehat{\mathrm{GLS}}} = \boldsymbol{C}(\boldsymbol{X}'\hat{\boldsymbol{V}}^{-1}\boldsymbol{X})^{-}\boldsymbol{X}'\hat{\boldsymbol{V}}^{-1}\boldsymbol{y}.$$

- In general,

$$\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\widehat{\mathrm{GLS}}} = \boldsymbol{C}(\boldsymbol{X}'\hat{\boldsymbol{V}}^{-1}\boldsymbol{X})^{-}\boldsymbol{X}'\hat{\boldsymbol{V}}^{-1}\boldsymbol{y}$$

is an nonlinear estimator that is an approximation to

$$\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\mathrm{GLS}} = \boldsymbol{C}(\boldsymbol{X}'\boldsymbol{V}^{-1}\boldsymbol{X})^{-}\boldsymbol{X}'\boldsymbol{V}^{-1}\boldsymbol{y},$$

which would be the BLUE of $\boldsymbol{C}\boldsymbol{\beta}$ if $\boldsymbol{V}$ were known.

- In special cases, $\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\widehat{\text{GLS}}}$ may be a linear estimator.

- For example, if there exists a matrix $\boldsymbol{Q}$ such that $\boldsymbol{VX} = \boldsymbol{XQ}$, then we know that

$$\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\text{GLS}} = \boldsymbol{C}\hat{\boldsymbol{\beta}} \quad \text{and} \quad \boldsymbol{C}\hat{\boldsymbol{\beta}}_{\widehat{\text{GLS}}} = \boldsymbol{C}\hat{\boldsymbol{\beta}},$$

which is a linear estimator of $\boldsymbol{C}\boldsymbol{\beta}$.

- However, even for our simple example involving seedling dry weight, $\boldsymbol{C}\hat{\boldsymbol{\beta}}_{\widehat{\text{GLS}}}$ is a nonlinear estimator of $\boldsymbol{C\beta}$ for

$$\begin{aligned}
\boldsymbol{C} = [1, 1, 0] &\iff \boldsymbol{C\beta} = \mu + \gamma_1, \\
\boldsymbol{C} = [1, 0, 1] &\iff \boldsymbol{C\beta} = \mu + \gamma_2, \text{ and} \\
\boldsymbol{C} = [0, 1, -1] &\iff \boldsymbol{C\beta} = \gamma_1 - \gamma_2.
\end{aligned}$$

- Confidence intervals and tests for these estimable functions are not exact.

- In our simple example involving seedling dry weight, there was only one random factor (pot).

- When there are m random factors, we can partition $\boldsymbol{Z}$ and $\boldsymbol{u}$ as

$$\boldsymbol{Z} = [\boldsymbol{Z}_1, \ldots, \boldsymbol{Z}_m] \text{ and } \boldsymbol{u} = \begin{bmatrix} \boldsymbol{u}_1 \\ \vdots \\ \boldsymbol{u}_m \end{bmatrix},$$

where $\boldsymbol{u}_j$ is the vector of random effects associated with factor j $(j = 1, \ldots, m)$.

- We can write $\boldsymbol{Zu}$ as

$$[\boldsymbol{Z}_1, \ldots, \boldsymbol{Z}_m] \begin{bmatrix} \boldsymbol{u}_1 \\ \vdots \\ \boldsymbol{u}_m \end{bmatrix} = \sum_{j=1}^{m} \boldsymbol{Z}_j \boldsymbol{u}_j.$$

- We often assume that all random effects (including random errors) are mutually independent and that the random effects associated with the jth random factor have variance σ_j^2 ($j = 1, \ldots, m$).

- Under these assumptions,

$$\mathrm{Var}(\boldsymbol{y}) = \boldsymbol{ZGZ}' + \boldsymbol{R} = \sum_{j=1}^{m} \sigma_j^2 \boldsymbol{Z}_j \boldsymbol{Z}_j' + \sigma_e^2 \boldsymbol{I}.$$

Example 2

- Consider an experiment involving 4 litters of 4 animals each.
- Suppose 4 treatments are randomly assigned to the 4 animals in each litter.
- Suppose we obtain two replicate muscle samples from each animal and measure the response of interest for each muscle sample.

Let y_{ijk} denote the kth measure of the response for the animal from litter j that received treatment i ($i = 1, 2, 3, 4; j = 1, 2, 3, 4; k = 1, 2$)

Suppose

$$y_{ijk} = \mu + \tau_i + \ell_j + a_{ij} + e_{ijk},$$

where

$$\boldsymbol{\beta} = [\mu, \tau_1, \tau_2, \tau_3, \tau_4]' \in \mathbb{R}^5$$

is an unknown vector of fixed parameters,

$$\boldsymbol{u} = [\ell_1, \ell_2, \ell_3, \ell_4, a_{11}, a_{21}, a_{31}, a_{41}, a_{12}, \ldots, a_{34}, a_{44}]'$$

is a vector of random effects, and

$$\boldsymbol{e} = [e_{111}, e_{112}, e_{212}, \ldots, e_{411}, e_{412}, \ldots, e_{441}, e_{442}]'$$

is a vector of random errors.

With

$$\boldsymbol{y} = [y_{111}, y_{112}, y_{212}, \ldots, y_{411}, y_{412}, \ldots, y_{441}, y_{442}]',$$

we can write the model as a linear mixed-effects model

$$\boldsymbol{y} = \boldsymbol{X\beta} + \boldsymbol{Zu} + \boldsymbol{e},$$

where

$$
\boldsymbol{X} = \begin{bmatrix}
1 & 1 & 0 & 0 & 0 \\
1 & 1 & 0 & 0 & 0 \\
1 & 0 & 1 & 0 & 0 \\
1 & 0 & 1 & 0 & 0 \\
1 & 0 & 0 & 1 & 0 \\
1 & 0 & 0 & 1 & 0 \\
1 & 0 & 0 & 0 & 1 \\
1 & 0 & 0 & 0 & 1 \\
\multicolumn{5}{c}{\text{The matrix}} \\
\multicolumn{5}{c}{\text{above repeated}} \\
\multicolumn{5}{c}{\text{three more}} \\
\multicolumn{5}{c}{\text{times.}}
\end{bmatrix}, \quad
\boldsymbol{Z} = \begin{bmatrix}
1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \dots & 0 \\
1 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & \dots & 0 \\
\vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \ddots & \vdots \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 1 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & \dots & 1
\end{bmatrix}
$$

We can write less and be more precise using Kronecker product notation.

$$\boldsymbol{X} = \underset{4\times 1}{\mathbf{1}} \otimes [\underset{8\times 1}{\mathbf{1}}, \underset{4\times 4}{\boldsymbol{I}} \otimes \underset{2\times 1}{\mathbf{1}}], \quad \boldsymbol{Z} = [\underset{4\times 4}{\boldsymbol{I}} \otimes \underset{8\times 1}{\mathbf{1}}, \underset{16\times 16}{\boldsymbol{I}} \otimes \underset{2\times 1}{\mathbf{1}}].$$

In this experiment, we have two random factors: litter and animal.

We can partition our random effects vector $\boldsymbol{u}$ into a vector of litter effects and a vector of animal effects:

$$\boldsymbol{u} = \begin{bmatrix} \boldsymbol{\ell} \\ \boldsymbol{a} \end{bmatrix}, \quad \boldsymbol{\ell} = \begin{bmatrix} \ell_1 \\ \ell_2 \\ \ell_3 \\ \ell_4 \end{bmatrix}, \quad \boldsymbol{a} = \begin{bmatrix} a_{11} \\ a_{21} \\ a_{31} \\ a_{41} \\ a_{12} \\ \vdots \\ a_{44} \end{bmatrix},$$

We make the usual assumption that

$$\boldsymbol{u} = \begin{bmatrix} \boldsymbol{\ell} \\ \boldsymbol{a} \end{bmatrix} \sim N\left(\begin{bmatrix} \boldsymbol{0} \\ \boldsymbol{0} \end{bmatrix}, \begin{bmatrix} \sigma_\ell^2 \boldsymbol{I} & \boldsymbol{0} \\ \boldsymbol{0} & \sigma_a^2 \boldsymbol{I} \end{bmatrix} \right),$$

where $\sigma_\ell^2, \sigma_a^2 \in \mathbb{R}^+$ are unknown parameters.

We can partition

$$\begin{aligned}
\boldsymbol{Z} &= [\underset{4\times 4}{\boldsymbol{I}} \otimes \underset{8\times 1}{\mathbf{1}}, \underset{16\times 16}{\boldsymbol{I}} \otimes \underset{2\times 1}{\mathbf{1}}] \\
&= [\mathbf{Z}_\ell, \mathbf{Z}_a].
\end{aligned}$$

We have

$$\begin{aligned}
\boldsymbol{Zu} &= [\mathbf{Z}_\ell, \mathbf{Z}_a] \begin{bmatrix} \boldsymbol{\ell} \\ \boldsymbol{a} \end{bmatrix} \\
&= \mathbf{Z}_\ell \boldsymbol{\ell} + \mathbf{Z}_a \boldsymbol{a}
\end{aligned}$$

and

$$
\begin{aligned}
\mathrm{Var}(\boldsymbol{Z}\boldsymbol{u}) &= \boldsymbol{Z}\boldsymbol{G}\boldsymbol{Z}' \\
&= [\boldsymbol{Z}_\ell, \boldsymbol{Z}_a] \begin{bmatrix} \sigma_\ell^2 \boldsymbol{I} & \boldsymbol{0} \\ \boldsymbol{0} & \sigma_a^2 \boldsymbol{I} \end{bmatrix} \begin{bmatrix} \boldsymbol{Z}_\ell' \\ \boldsymbol{Z}_a' \end{bmatrix} \\
&= \boldsymbol{Z}_\ell(\sigma_\ell^2 \boldsymbol{I})\boldsymbol{Z}_\ell' + \boldsymbol{Z}_a(\sigma_a^2 \boldsymbol{I})\boldsymbol{Z}_a' \\
&= \sigma_\ell^2 \boldsymbol{Z}_\ell \boldsymbol{Z}_\ell' + \sigma_a^2 \boldsymbol{Z}_a \boldsymbol{Z}_a' \\
&= \sigma_\ell^2 \underset{4\times 4}{\boldsymbol{I}} \otimes \underset{8\times 8}{\boldsymbol{1}\boldsymbol{1}'} + \sigma_a^2 \underset{16\times 16}{\boldsymbol{I}} \otimes \underset{2\times 2}{\boldsymbol{1}\boldsymbol{1}'}.
\end{aligned}
$$

We usually assume that all random effects and random errors are mutually independent and that the errors (like the effects within each factor) are identically distributed:

$$\begin{bmatrix} \boldsymbol{\ell} \\ \boldsymbol{a} \\ \boldsymbol{e} \end{bmatrix} \sim N\left(\begin{bmatrix} \mathbf{0} \\ \mathbf{0} \\ \mathbf{0} \end{bmatrix}, \begin{bmatrix} \sigma_\ell^2 \boldsymbol{I} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \sigma_a^2 \boldsymbol{I} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \sigma_e^2 \boldsymbol{I} \end{bmatrix} \right).$$

The unknown variance parameters $\sigma_\ell^2, \sigma_a^2, \sigma_e^2 \in \mathbb{R}^+$ are called <u>variance components</u>.

In this case, we have $\boldsymbol{R} = \mathrm{Var}(\boldsymbol{e}) = \sigma_e^2 \boldsymbol{I}$.

Thus,

$$\begin{aligned} \mathrm{Var}(\boldsymbol{y}) &= \boldsymbol{ZGZ}' + \boldsymbol{R} \\ &= \sigma_\ell^2 \boldsymbol{Z}_\ell \boldsymbol{Z}_\ell' + \sigma_a^2 \boldsymbol{Z}_a \boldsymbol{Z}_a' + \sigma_e^2 \boldsymbol{I}. \end{aligned}$$

This is a block diagonal matrix with a block as follows.

(To get a block to fit on one slide, let $\ell = \sigma_\ell^2, a = \sigma_a^2, e = \sigma_e^2$).

$$
\begin{array}{cccccccc}
\ell+a+e & \ell+a & \ell & \ell & \ell & \ell & \ell & \ell \\
\ell+a & \ell+a+e & \ell & \ell & \ell & \ell & \ell & \ell \\
\ell & \ell & \ell+a+e & \ell+a & \ell & \ell & \ell & \ell \\
\ell & \ell & \ell+a & \ell+a+e & \ell & \ell & \ell & \ell \\
\ell & \ell & \ell & \ell & \ell+a+e & \ell+a & \ell & \ell \\
\ell & \ell & \ell & \ell & \ell+a & \ell+a+e & \ell & \ell \\
\ell & \ell & \ell & \ell & \ell & \ell & \ell+a+e & \ell+a \\
\ell & \ell & \ell & \ell & \ell & \ell & \ell+a & \ell+a+e
\end{array}
$$