

# 1 Off-Diagonal Components in Roy's Model

The Within-item variability is specified as follows, where  $x$  and  $y$  are the methods of measurement in question.

$$\begin{pmatrix} \sigma_x^2 & \sigma_{xy} \\ \sigma_{xy} & \sigma_y^2 \end{pmatrix}$$

$\sigma_x^2$  and  $\sigma_y^2$  describe the level of measurement error associated with each of the measurement methods for a given item. Attention must be given to the off-diagonal elements of the matrix.

It is intuitive to consider the measurement error of the two methods as independent of each other.

## 2 Formal Testing

A formal test can be performed to test the hypothesis that the off-diagonal terms are zero.

$$\begin{pmatrix} \sigma_x^2 & \sigma_{xy} \\ \sigma_{xy} & \sigma_y^2 \end{pmatrix} vs \begin{pmatrix} \sigma_x^2 & 0 \\ 0 & \sigma_y^2 \end{pmatrix}$$

## 3 Basic Models Fits

Further to Pinheiro and Bates (1994), several simple LME models are constructed for the blood pressure data. This data set is the subject of a method comparison study in Bland and Altman (1999).

### 3.1 Implementing the Mixed Models Fits

They are implemented using the following R code, utilising the 'nlme' package. An analysis of variance is used to compare the model fits.

The R script:

```
fit1 = lme( BP ~ method, data = dat, random = ~1 | subject )
fit2 = update(fit1, random = ~1 | subject/method )
fit3 = update(fit1, random = ~method - 1 | subject )
#analysis of variance
anova(fit1,fit2,fit3)
```

1. Simplest workable model, allows differences between methods and incorporates a

random intercept for each subject. For subject 1 we have

$$\mathbf{X}_i = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 1 & 1 \\ 1 & 1 \\ 1 & 1 \end{pmatrix}, \quad \boldsymbol{\beta} = \begin{pmatrix} \beta_0 \\ \beta_1 \end{pmatrix}, \quad \mathbf{Z}_i = \begin{pmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{pmatrix}, \quad \mathbf{b}_i = b$$

where  $E(b) = 0$  and  $\text{var}(b) = \psi$ .

2.

$$\mathbf{Z}_i = \begin{pmatrix} 1 & 0 \\ 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix} \quad \mathbf{b}_i = \begin{pmatrix} b_1 & 0 \\ 0 & b_2 \end{pmatrix}$$

where  $E(b_i) = 0$  and  $\text{var}(\mathbf{b}) = \boldsymbol{\Psi}$ .

The variance of error terms is a  $6 \times 6$  matrix.

### 3.2 Model Fit 1

This is a simple model with no interactions. There is a fixed effect for each method and a random effect for each subject.

$$y_{ijk} = \beta_j + b_i + \epsilon_{ijk}, \quad i = 1, \dots, 2, j = 1, \dots, 85, k = 1, \dots, 3$$

$$b_i \sim \mathcal{N}(0, \sigma_b^2), \quad \epsilon_i \sim \mathcal{N}(0, \sigma^2)$$

Linear mixed-effects model fit by REML

Data: dat

Log-restricted-likelihood: -2155.853

Fixed: BP ~ method

(Intercept)      methodS

127.40784      15.61961

Random effects:

Formula: ~1 | subject

(Intercept) Residual

StdDev:      29.39085 12.44454

Number of Observations: 510

Number of Groups: 85

### 3.3 Model Fit 2

This is a simple model, this time with an interaction effect. There is a fixed effect for each method. This model has random effects at two levels  $b_i$  for the subject, and another,  $b_{ij}$ , for the respective method within each subject.

$$y_{ijk} = \beta_j + b_i + b_{ij} + \epsilon_{ijk}, \quad i = 1, \dots, 2, j = 1, \dots, 85, k = 1, \dots, 3$$

$$b_i \sim \mathcal{N}(0, \sigma_1^2), \quad b_{ij} \sim \mathcal{N}(0, \sigma_2^2), \quad \epsilon_i \sim \mathcal{N}(0, \sigma^2)$$

In this model, the random interaction terms all have the same variance  $\sigma_2^2$ . These terms are assumed to be independent of each other, even within the same subject.

Linear mixed-effects model fit by REML

Data: dat

Log-restricted-likelihood: -2047.714

Fixed: BP ~ method

(Intercept)      methodS

127.40784      15.61961

Random effects:

Formula: ~1 | subject

(Intercept)

StdDev:      28.28452

Formula: ~1 | method %in% subject

(Intercept) Residual

StdDev:      12.61562 7.763666

Number of Observations: 510

Number of Groups:

subject method %in% subject

85                      170

### 3.4 Model Fit 3

This model is a more general model, compared to 'model fit 2'. This model treats the random interactions for each subject as a vector and allows the variance-covariance matrix for that vector to be estimated from the set of all positive-definite matrices.  $\mathbf{y}_i$  is the entire response vector for the  $i$ th subject.  $\mathbf{X}_i$  and  $\mathbf{Z}_i$  are the fixed- and random-effects design matrices respectively.

$$\mathbf{y}_i = \mathbf{X}_i \boldsymbol{\beta} + \mathbf{Z}_i \mathbf{b}_i + \boldsymbol{\epsilon}_i, \quad i = 1, \dots, 85$$

observation	BP	subject	method	replicate
1	100.00	1	J	1
86	106.00	1	J	2
171	107.00	1	J	3
511	122.00	1	S	1
596	128.00	1	S	2
681	124.00	1	S	3

$$\mathbf{Z}_i \sim \mathcal{N}(\mathbf{0}, \Psi), \quad \boldsymbol{\epsilon}_i \sim \mathcal{N}(\mathbf{0}, \sigma^2 \Lambda)$$

For the first subject the response vector,  $\mathbf{y}_1$ , is: The fixed effects design matrix  $\mathbf{X}_i$  is given by:

(Intercept)	method S
1	0
1	0
1	0
1	1
1	1
1	1

The random effects design matrix  $\mathbf{Z}_i$  is given by: The following output was ob-

method J	method S
1	0
1	0
1	0
0	1
0	1
0	1

tained.

```
Linear mixed-effects model fit by REML
Data: dat
Log-restricted-likelihood: -2047.582
Fixed: BP ~ method
(Intercept)      methodS
127.40784      15.61961
```

```

Random effects:
Formula: ~method - 1 | subject
Structure: General positive-definite, Log-Cholesky parametrization
StdDev      Corr
methodJ    30.455093 methodJ
methodS    31.477237 0.835
Residual   7.763666

```

Number of Observations: 510

Number of Groups: 85

### 3.5 Extended LME model

The extended single level LME model relaxes the independence assumption, allowing heteroscedastic and correlated within group errors.

$$\epsilon_i = \mathcal{N}(0, \sigma^2 \Lambda_i) \quad (1)$$

$\Lambda_i$  are positive definite matrices.  $\sigma^2$  is factored out of the matrix for computational reasons.

## 4 Variance functions

Variance functions are applied to LME models through the ‘weights’ argument. *R* supports several variance functions.

‘varIdent’ constructs a model with different variances per stratum.

### 4.1 Diagnostic plots

Diagnostic plots for identifying within-group heteroscedascity and assessing the adequacy of a variance function can also be used with ‘nlme’ objects.

## References

- Bland, J. and D. Altman (1999). Measuring agreement in method comparison studies. *Statistical Methods in Medical Research* 8(2), 135–160.
- Pinheiro, J. and D. Bates (1994). *Mixed Effects Models in S and S plus* (2nd ed.). Reading, Massachusetts: Springer.