Chapter 1

Appendix C

1.1 Demonstration of Roy's Model

Roy (2009) proposes a LME based approach with Kronecker product covariance structure with doubly multivariate setup to assess the agreement between two methods. By doubly multivariate set up, Roy means that the information on each patient or item is multivariate at two levels, the number of methods and number of replicated measurements. Further to Lam et al. (1999), it is assumed that the replicates are linked over time. However it is easy to modify to the unlinked case. This approachs allows for unbalanced data, i.e. unequal numbers of replications for each subject.

Response for ith subject can be written as

$$y_i = \beta_0 + \beta_1 x_{i1} + \beta_2 x_{i2} + b_{1i} z_{i1} + b_{2i} z_{i2} + \epsilon_i$$

- β_1 and β_2 are fixed effects corresponding to both methods. (β_0 is the intercept.)

- b_{1i} and b_{2i} are random effects corresponding to both methods.

Overall variability between the two methods (Ω) is sum of between-subject (G) and within-subject variability (Σ),

$$\text{Block } \mathbf{\Omega}_i = \begin{bmatrix} d_1^2 & d_{12} \\ d_{12} & d_2^2 \end{bmatrix} + \begin{bmatrix} \sigma_1^2 & \sigma_{12} \\ \sigma_{12} & \sigma_2^2 \end{bmatrix}.$$

In order to express Roy's LME model in matrix notation we gather all $2n_i$ observations specific to item i into a single vector $\boldsymbol{y}_i = (y_{1i1}, y_{2i1}, y_{1i2}, \ldots, y_{mir}, \ldots, y_{1in_i}, y_{2in_i})'$. The LME model can be written

$$\boldsymbol{y}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{b}_i + \boldsymbol{\epsilon}_i,$$

where $\boldsymbol{\beta} = (\beta_0, \beta_1, \beta_2)'$ is a vector of fixed effects, and $\boldsymbol{X}_i$ is a corresponding $2n_i \times 3$ design matrix for the fixed effects. The random effects are expressed in the vector $\boldsymbol{b} = (b_1, b_2)'$, with $\boldsymbol{Z}_i$ the corresponding $2n_i \times 2$ design matrix. The vector $\boldsymbol{\epsilon}_i$ is a $2n_i \times 1$ vector of residual terms.

It is assumed that $\boldsymbol{b}_i \sim N(0, \boldsymbol{G})$, $\boldsymbol{\epsilon}_i$ is a matrix of random errors distributed as $N(0, \boldsymbol{R}_i)$ and that the random effects and residuals are independent of each other.

The maximum likelihood estimate of the between-subject variance covariance matrix of two methods is given as G. The estimate for the within-subject variance covariance matrix is $\hat{\Sigma}$. The estimated overall variance covariance matrix 'Block Ω_i' is the addition of $\hat{G}$ and $\hat{\Sigma}$.

$$\text{Block } \Omega_i = \hat{G} + \hat{\Sigma} \tag{1.1}$$

$\boldsymbol{G}$ is the variance covariance matrix for the random effects $\boldsymbol{b}$. i.e. between-item sources of variation. The between-item variance covariance matrix $\boldsymbol{G}$ is constructed as follows:

$$\text{Var} \begin{bmatrix} b_1 \\ b_2 \end{bmatrix} = \boldsymbol{G} = \begin{pmatrix} g_1^2 & g_{12} \\ g_{12} & g_2^2 \end{pmatrix}$$

It is important to note that no special assumptions about the structure of $\boldsymbol{G}$ are made. An example of such an assumption would be that $\boldsymbol{G}$ is the product of a scalar value and the identity matrix.

$\boldsymbol{R}_i$ is the variance covariance matrix for the residuals, i.e. the within-item sources of variation between both methods. Computational analysis of linear mixed effects models allow for the explicit analysis of both $\boldsymbol{G}$ and $\boldsymbol{R}_i$.

The overall variability between the two methods is the sum of between-item variability $\boldsymbol{G}$ and within-item variability $\boldsymbol{\Sigma}$. Roy (2009) denotes the overall variability as Block - $\boldsymbol{\Omega}_i$. The overall variation for methods 1 and 2 are given by

$$\begin{pmatrix} \omega_1^2 & \omega_{12} \\ \omega_{12} & \omega_2^2 \end{pmatrix} = \begin{pmatrix} g_1^2 & g_{12} \\ g_{12} & g_2^2 \end{pmatrix} + \begin{pmatrix} \sigma_1^2 & \sigma_{12} \\ \sigma_{12} & \sigma_2^2 \end{pmatrix}$$

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. $\boldsymbol{y_i}$ is the entire response vector for the ith subject. $\boldsymbol{X_i}$ and $\boldsymbol{Z_i}$ are the fixed- and random-effects design matrices respectively.

$$\boldsymbol{y_i} = \boldsymbol{X_i\beta} + \boldsymbol{Z_i b_i} + \boldsymbol{\epsilon_i}, \qquad i = 1, \ldots, 85$$

$$\boldsymbol{Z_i} \sim \mathcal{N}(\boldsymbol{0}, \boldsymbol{\Psi}), \qquad \boldsymbol{\epsilon_i} \sim \mathcal{N}(\boldsymbol{0}, \boldsymbol{\sigma^2 \Lambda})$$

Roy (2009) presents two nested models that specify the condition of equality as required, with a third nested model for an additional test. There three formulations share the same structure, and can be specified by making slight alterations of the code for the Reference Model.

For these tests, four candidate LME models are constructed. The differences in the models are specifically in how the the $\boldsymbol{G}$ and Λ matrices are constructed, using either an unstructured form or a compound symmetry form. To illustrate these differences, consider a generic matrix A,

$$\boldsymbol{A} = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}.$$

A symmetric matrix allows the diagonal terms a_{11} and a_{22} to differ. The compound symmetry structure requires that both of these terms be equal, i.e $a_{11} = a_{22}$.

1.1.1 Test 1

1.2   Issue of Tractability

Bibliography

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