

Contents

| | | |
|----------|--|----------|
| 1 | Why use LMEs for Method Comparison? | 1 |
| 2 | Two-tailed testing | 2 |
| 3 | One Tailed Testing | 2 |
| 4 | Enabling One Tailed Testing | 3 |
| 5 | Profile Likelihood | 4 |
| 6 | Implementation of PL Confidence Intervals | 4 |

1 Why use LMEs for Method Comparison?

The LME model approach has seen increased use as a framework for method comparison studies in recent years (Lai & Shaio, Carstensen and Choudhary as examples). In part this is due to the increased profile of LME models, and furthermore the availability of capable software. Additionally LME based approaches may utilise the diagnostic and influence analysis techniques that have been developed in recent times.

Roy proposes an LME model with Kronecker product covariance structure in a doubly multivariate setup. Response for i th 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 (D) and

within-subject variability (Σ),

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

The well-known “Limits of Agreement”, as developed by Bland and Altman (1986) are easily computable using the LME framework, proposed by Roy. While we will not be considering this analysis, a demonstration will be provided in the example.

Further to this, Roy(2009) demonstrates an suite of tests that can be used to determine how well two methods of measurement, in the presence of repeated measures, agree with each other.

- No Significant inter-method bias
- No difference in the between-subject variabilities of the two methods
- No difference in the within-subject variabilities of the two methods

2 Two-tailed testing

A test for equality of variances, based on the likelihood Ratio test, is very simple to implement using existing methodologies. All that is required it to specify the reference model and the relevant nested mode as arguments to the command `anova()`. The output can be interpreted in the usual way.

3 One Tailed Testing

The approach proposed by Roy deals with the question of agreement, and indeed interchangeability, as developed by Bland and Altman’s corpus of work. In the view of

Dunn, a question relevant to many practitioners is which of the two methods is more precise.

The relationship between precision and the within-item and between-item variability must be established. Roy establishes the equivalence of repeatability and within-item variability, and hence precision. The method with the smaller within-item variability can be deemed to be the more precise.

4 Enabling One Tailed Testing

A useful approach is to compute the confidence intervals for the ratio of within-item standard deviations (equivalent to the ratio of repeatability coefficients), which can be interpreted in the usual manner (or alternatively, the ratio of the variances). In fact, the ratio of within-item standard deviations, with the attendant confidence interval, can be determined using a single R command: `intervals()`.

Pinheiro and Bates (pg 93-95) give a description of how confidence intervals for the variance components are computed. Furthermore a complete set of confidence intervals can be computed to complement the variance component estimates. However, to facilitate one tailed testing, What is required is the computation of the variance ratios of within-item and between-item standard deviations.

A nave approach would be to compute the variance ratios by relevant F distribution quantiles. However, the question arises as to the appropriate degrees of freedom. However, Douglas Bates has stated that an alternative approach is required (i.e. Profile Likelihoods)

”The omission of standard errors on variance components is intentional.

The distribution of an estimator of a variance component is highly skewed and obtaining an estimate of the standard deviation of a skewed distribu-

tion is not very useful. A much better approach is based on profiling the objective function.” (Douglas Bates May 2012)

5 Profile Likelihood

Normal-based confidence intervals for a parameter of interest are inaccurate when the sampling distribution of the estimate is skewed. The technique known as profile likelihood can produce confidence intervals with better coverage. It may be used when the model includes only the variable of interest or several other variables in addition. Profile-likelihood confidence intervals are particularly useful in nonlinear models.

Profile likelihood confidence intervals are based on the log-likelihood function.

6 Implementation of PL Confidence Intervals

The suitable calculation of confidence limits for this variance ratio are to be computed using the profile likelihood approach. The R package `profilelikelihood` will be assessed for feasibility, particularly the command `profilelikelihood.lme()`