Residual Analysis for LME Models in the MCS context

Kevin O'Brien

November 25, 2014

- `R` command and `R` object - Typewriter Font
- `R` Package name - Italics
- Selected Acronyms and Proper Nouns - Italics

0.1 What is Influence

Broadly defined, influence is understood as the ability of a single or multiple data points, through their presence or absence in the data, to alter important aspects of the analysis, yield qualitatively different inferences, or violate assumptions of the statistical model. The goal of influence analysis is not primarily to mark data points for deletion so that a better model fit can be achieved for the reduced data, although this might be a result of influence analysis *schabenberger*.

0.2 Quantifying Influence

The basic procedure for quantifying influence is simple as follows:

- Fit the model to the data and obtain estimates of all parameters.
- Remove one or more data points from the analysis and compute updated estimates of model parameters.
- Based on full- and reduced-data estimates, contrast quantities of interest to determine how the absence of the observations changes the analysis.

cook86 introduces powerful tools for local-influence assessment and examining perturbations in the assumptions of a model. In particular the effect of local perturbations of parameters or observations are examined.

1 Extension of techniques to LME Models

Model diagnostic techniques, well established for classical models, have since been adapted for use with linear mixed effects models.Diagnostic techniques for LME models are inevitably more difficult to implement, due to the increased complexity.

Beckman, Nachtsheim and Cook (1987) Beckman applied the local influence method of Cook (1986) to the analysis of the linear mixed model.

While the concept of influence analysis is straightforward, implementation in mixed models is more complex. Update formulae for fixed effects models are available only when the covariance parameters are assumed to be known.

If the global measure suggests that the points in U are influential, the nature of that influence should be determined. In particular, the points in U can affect the following

- the estimates of fixed effects,
- the estimates of the precision of the fixed effects,
- the estimates of the covariance parameters,
- the estimates of the precision of the covariance parameters,
- fitted and predicted values.

2 Conditional and Marginal Residuals

Conditional residuals include contributions from both fixed and random effects, whereas marginal residuals include contribution from only fixed effects.

Suppose the linear mixed-effects model lmehas an n-by-p fixed-effects design matrix X and an n-by-q random-effects design matrix Z.

$$\hat{y}_{Cond} = X\hat{\beta} + Z\hat{b}$$

and the fitted marginal response is

$$\hat{y}_{Mar} = X\hat{\beta}$$

residuals can return three types of residuals: raw, Pearson, and standardized. For any type, you can compute the conditional or the marginal residuals. For example, the conditional raw residual is

$$r_{Cond} = y - X\hat{\beta} - Z\hat{b}$$

and the marginal raw residual is

$$r_{Mar} = y - X\hat{\beta}$$

Marginal residuals:

$$y - X\beta = Z\eta + \epsilon$$

- Should be mean 0, but may show grouping structure
- May not be homoskedastic!
- Good for checking fixed effects, just like linear regr.

Conditional residuals:

$$y - X\beta - Z\eta = \epsilon$$

- Should be mean zero with no grouping structure
- Should be homoskedastic!
- Good for checking normality of outliers

Random effects:

$$y - X\beta - \epsilon = Z\eta$$

- Should be mean zero with no grouping structure
- May not be be homoskedastic!

Diagnostic Methods for OLS models

Influence diagnostics are formal techniques allowing for the identification of observations that exert substantial influence on the estimates of fixed effects and variance covariance parameters.

The idea of influence diagnostics for a given observation is to quantify the effect of omission of this observation from the data on the results of the model fit. To this aim, the concept of likelihood displacement is used.

Influence Diagnostics: Basic Idea and Statistics

The general idea of quantifying the influence of one or more observations relies on computing parameter estimates based on all data points, removing the cases in question from the data, refitting the model, and computing statistics based on the change between full-data and reduced-data estimation.

3 Case Deletion Diagnostics

CPJ develops case deletion diagnostics, in particular the equivalent of Cook's distance, for diagnosing influential observations when estimating the fixed effect parameters and variance components.

3.1 Deletion Diagnostics

Since the pioneering work of Cook in 1977, deletion measures have been applied to many statistical models for identifying influential observations.

Deletion diagnostics provide a means of assessing the influence of an observation (or groups of observations) on inference on the estimated parameters of LME models.

Data from single individuals, or a small group of subjects may influence non-linear mixed effects model selection. Diagnostics routinely applied in model building may identify such individuals, but these methods are not specifically designed for that purpose and are, therefore, not optimal. We describe two likelihood-based diagnostics for identifying individuals that can influence the choice between two competing models.

Case-deletion diagnostics provide a useful tool for identifying influential observations and outliers.

The computation of case deletion diagnostics in the classical model is made simple by the fact that estimates of β and σ^2, which exclude the ith observation, can be computed without re-fitting the model. Such update formulas are available in the mixed model only if you assume that the covariance parameters are not affected by the removal of the observation in question. This is rarely a reasonable assumption.

4 Effects on fitted and predicted values

$$\hat{e}_{i(U)} = y_i - x\hat{\beta}_{(U)} \tag{1}$$

Cook's Distance

Cook (1977) greatly expanded the study of residuals and influence measures. Cook's key observation was the effects of deleting each observation in turn could be computed without undue additional computational expense. Consequently deletion diagnostics have become an integral part of assessing linear models.

Cook (1986) gave a completely general method for assessing influence of local departures from assumptions in statistical models.

Cook's Distance

In classical linear regression, a commonly used meausre of influence is Cook's distance. It is used as a measure of influence on the regression coefficients.

Cook's Distance

Cooks Distance (D_i) is an overall measure of the combined impact of the ith case of all estimated regression coefficients. It uses the same structure for measuring the combined impact of the differences in the estimated regression coefficients when the $i-$th case is deleted.

Importantly, $D_{(i)}$ can be calculated without fitting a new regression coefficient each time an observation is deleted.

4.1 Cooks's Distance

Cook's D statistics (i.e. colloquially Cook's Distance) is a measure of the influence of observations in subset U on a vector of parameter estimates.

$$\delta_{(U)} = \hat{\beta} - \hat{\beta}_{(U)}$$

If V is known, Cook's D can be calibrated according to a chi-square distribution with degrees of freedom equal to the rank of $\boldsymbol{X}$.

For LME models, Cook's distance can be extended to model influence diagnostics by definining.

It is also desirable to measure the influence of the case deletions on the covariance matrix of $\hat{\beta}$.

5 Cook's Distance for LMEs

Cook's Distance is a well known diagnostic technique used in classical linear models, extended to LME models. For LME models, two formulations exist; a Cook's distance that examines the change in fixed fixed parameter estimates, and another that examines the change in random effects parameter estimates. The outcome of either Cook's distance is a scaled change in either β or θ.

Diagnostic methods for fixed effects are generally analogues of methods used in classical linear models. Diagnostic methods for variance components are based on 'one-step' methods. *Cook (1986)* gives a completely general method for assessing the influence of local departures from assumptions in statistical models.

For fixed effects parameter estimates in LME models, the Cook's distance can be extended to measure influence on these fixed effects.

$$\mathrm{CD}_i(\beta) = \frac{(c_{ii} - r_{ii}) \times t_i^2}{r_{ii} \times p}$$

For random effect estimates, the Cook's distance is

$$\mathrm{CD}_i(b) = g\prime_{(i)}(I_r + \mathrm{var}(\hat{b})D)^{-2}\mathrm{var}(\hat{b})g_{(i)}.$$

Large values for Cook's distance indicate observations for special attention.

5.1 Change in the precision of estimates

The effect on the precision of estimates is separate from the effect on the point estimates. Data points that have a small Cook's distance, for example, can still greatly affect hypothesis tests and confidence intervals, if their influence on the precision of the estimates is large.

Influence Analysis for LME Models

The linear mixed effects model is a useful methodology for fitting a wide range of models. However, linear mixed effects models are known to be sensitive to outliers. Christensen et al advises that identification of outliers is necessary before conclusions may be drawn from the fitted model.

Standard statistical packages concentrate on calculating and testing parameter estimates without considering the diagnostics of the model.The assessment of the effects of perturbations in data, on the outcome of the analysis, is known as statistical influence analysis. Influence analysis examines the robustness of the model. Influence analysis methodologies have been used extensively in classical linear models, and provided the basis for methodologies for use with LME models. Computationally inexpensive diagnostics tools have been developed to examine the issue of influence (Zewotir). Studentized residuals, error contrast matrices and the inverse of the response variance covariance matrix are regular components of these tools.

Influence Statistics for LME models

Influence statistics can be coarsely grouped by the aspect of estimation that is their primary target:

- overall measures compare changes in objective functions: (restricted) likelihood distance (Cook and Weisberg 1982, Ch. 5.2)
- influence on parameter estimates: Cook's (Cook 1977, 1979), MDFFITS (Belsley, Kuh, and Welsch 1980, p. 32)
- influence on precision of estimates: CovRatio and CovTrace
- influence on fitted and predicted values: PRESS residual, PRESS statistic (Allen 1974), DFFITS (Belsley, Kuh, and Welsch 1980, p. 15)
- outlier properties: internally and externally studentized residuals, leverage

Influence Analysis for LME Models

The linear mixed effects model is a useful methodology for fitting a wide range of models. However, linear mixed effects models are known to be sensitive to outliers. Christensen et al. advises that identification of outliers is necessary before conclusions may be drawn from the fitted model.

Standard statistical packages concentrate on calculating and testing parameter estimates without considering the diagnostics of the model.The assessment of the effects of perturbations in data, on the outcome of the analysis, is known as statistical influence analysis. Influence analysis examines the robustness of the model. Influence analysis methodologies have been used extensively in classical linear models, and provided the basis for methodologies for use with LME models. Computationally inexpensive diagnostics tools have been developed to examine the issue of influence (Zewotir). Studentized residuals, error contrast matrices and the inverse of the response variance covariance matrix are regular components of these tools.

Influence Statistics for LME models

Influence statistics can be coarsely grouped by the aspect of estimation that is their primary target:

- overall measures compare changes in objective functions: (restricted) likelihood distance (Cook and Weisberg 1982, Ch. 5.2)
- influence on parameter estimates: Cook's (Cook 1977, 1979), MDFFITS (Belsley, Kuh, and Welsch 1980, p. 32)
- influence on precision of estimates: CovRatio and CovTrace
- influence on fitted and predicted values: PRESS residual, PRESS statistic (Allen 1974), DFFITS (Belsley, Kuh, and Welsch 1980, p. 15)

- outlier properties: internally and externally studentized residuals, leverage

schabenberger examines the use and implementation of influence measures in LME models.

Influence is understood to be the ability of a single or multiple data points, through their presences or absence in the data, to alter important aspects of the analysis, yield qualitatively different inferences, or violate assumptions of the statistical model (*schabenberger*).

Outliers are the most noteworthy data points in an analysis, and an objective of influence analysis is how influential they are, and the manner in which they are influential.

schabenberger describes a simple procedure for quantifying influence. Firstly a model should be fitted to the data, and estimates of the parameters should be obtained. The second step is that either single of multiple data points, specifically outliers, should be omitted from the analysis, with the original parameter estimates being updated. This is known as 'leave one out leave k out' analysis. The final step of the procedure is comparing the sets of estimates computed from the entire and reduced data sets to determine whether the absence of observations changed the analysis.

A residual is the difference between an observed quantity and its estimated or predicted value. In LME models, there are two types of residuals, marginal residuals and conditional residuals. A marginal residual is the difference between the observed data and the estimated marginal mean. A conditional residual is the difference between the observed data and the predicted value of the observation. In a model without random effects, both sets of residuals coincide.

schabenberger notes that it is not always possible to derive influence statistics necessary for comparing full- and reduced-data parameter estimates.

Abstract

This paper reviews the use of diagnostic measures for LME models in SAS. This text has been widely cited by texts that don't deal with SAS implementations.

Schabenberger: Summary and Conclusions

- Standard residual and inuence diagnostics for linear models can be extended to linear mixed models. The dependence of xed-effects solutions on the covariance parameter estimates has important ramications in perturbation analysis.
- To gauge the full impact of a set of observations on the analysis, covariance parameters need to be updated, which requires retting of the model.
- The experimental INFLUENCE option of the MODEL statement in the MIXED procedure (SAS 9.1) enables you to perform iterative and noniterative inuence analysis for individual observations and sets of observations.

- The conditional (subject-specic) and marginal (population-averaged) formulations in the linear mixed model enable you to consider conditional residuals that use the estimated BLUPs of the random effects, and marginal residuals which are deviations from the overall mean.

- Residuals using the BLUPs are useful to diagnose whether the random effects components in the model are specied correctly, marginal residuals are useful to diagnose the xed-effects components.

- Both types of residuals are available in SAS 9.1 as an experimental option of the MODEL statement in the MIXED procedure.

- It is important to note that influence analyses are performed under the assumption that the chosen model is correct. Changing the model structure can alter the conclusions. Many other variance models have been t to the data presented in the repeated measures example. You need to see the conclusions about which model component is affected in light of the model being fit.

- For example, modeling these data with a random intercept and random slope for each child or an unstructured covariance matrix will affect your conclusions about which children are inuential on the analysis and how this influence manifests itself.

6 CPJ's Three Propositions

6.0.1 Proposition 1

$$\boldsymbol{V}^{-1} = \begin{bmatrix} \nu^{ii} & \lambda_i' \\ \lambda_i & \Lambda_{[i]} \end{bmatrix}$$

$$\boldsymbol{V}_{[i]}^{-1} = \boldsymbol{\Lambda}_{[i]} - \frac{\lambda_i \lambda_i'}{\lambda_i}$$

6.1 Proposition 2

(i) $\boldsymbol{X}_{[i]}^T \boldsymbol{V}_{[i]}^{-1} \boldsymbol{X}_{[i]} = \boldsymbol{X}' \boldsymbol{V}^{-1} \boldsymbol{X}$

(ii) $= (\boldsymbol{X}' \boldsymbol{V}^{-1} \boldsymbol{Y})^{-1}$

(iii) $\boldsymbol{X}_{[i]}^T \boldsymbol{V}_{[i]}^{-1} \boldsymbol{Y}_{[i]} = \boldsymbol{X}' \boldsymbol{V}^{-1} \boldsymbol{Y}$

6.2 Proposition 3

This proposition is similar to the formula for the one-step Newtown Raphson estimate of the logistic regression coefficients given by Pregibon (1981) and discussed in Cook Weisberg.

- *The previous Section (Section 4) is a literary review of residual diagnostics and influence procedures for Linear Mixed Effects Models, drawing heavily on Schabenberger and Zewotir.*

- *Section 4 begins with an introduction to key topics in residual diagnostics, such as influence, leverage, outliers and Cook's distance. Other concepts such as DFFITS and DFBETAs will be introduced briefly, mostly to explain why the are not particularly useful for the Method Comparison context, and therefore are not elaborated upon.*

- *In brief, Variable Selection is not applicable to Method Comparison Studies, in the commonly used used context. Testing a rather simplisticy specificied model against one with more random effects terms is tractable, but this research question is of secondary importance.*

Appendix to Section 4

As an appendix to section 4, an appraisal of the current state of development (or lack thereof) for current implemenations for LME models, particularly for `nlme` and `lme4` fitted models.

Crucially, a review of internet resources indicates that almost all of the progress in this regard has been done for `lme4` fitted models, specifically the *Influence.ME* `R` package. (Nieuwenhuis et 2012)

Conversely there is very little for `nlme` models. To delve into this mor, one would immediately investigate the current development workflow for both packages.

As an aside, Douglas Bates was arguably the most prominent `R` developer working in the LME area. However Bates has now prioritised the development of LME models in another computing environment , i.e Julia.

The `nlme` package

With regards to `nlme`, the torch has been passed to Galecki Galecki & Burzykowski (UMich. and Hasselt respecitely). Galecki & Burzykowski published *Linear Mixed Effects Models using R*. Also, the accompanying `R` package, nlmeU package is under current development, with a version being released XXXX.

The `lme4` package

The `lme4` package is also under active development, under the leadership of Ben Bolker (McMaster University). According to CRAN, the LME4 package, fits linear and generalized linear mixed-effects models

> The models and their components are represented using S4 classes and methods. The core computational algorithms are implemented using the Eigen C++ library for numerical linear algebra and RcppEigen "glue". (CRAN)

The key issue is that `nlme` allows for the particular specification of Roy's Model, speciifically direct spefiication of the VC matrices for within subject and between subject residuals. The `lme4` package does not allow for this. To advance the ideas that eminate from Roys' paper, one is required to use the `nlme` context. However, to take advantage of the infrastructure already provided for `lme4` models, one may change the research question away from that of Roy's paper. To this end, an exploration of what textitinfluence.ME can accomplished is merited. As a complement to this, one can also consider how to properly employ the R^2 measure, in the context of Methoc Comparison Studies, further to the work by Edwards et al, namely "An R^2 statistic for fixed effects in the linear mixed model".

Abstract for "An R^2 statistic for fixed effects in the linear mixed model" Statisticians most often use the linear mixed model to analyze Gaussian longitudinal data.

The value and familiarity of the R2 statistic in the linear univariate model naturally creates great interest in extending it to the linear mixed model. We define and describe how to compute a model R2 statistic for the linear mixed model by using only a single model.

The proposed R2 statistic measures multivariate association between the repeated outcomes and the fixed effects in the linear mixed model. The R2 statistic arises as a 11 function of an appropriate F statistic for testing all fixed effects (except typically the intercept) in a full model.

The statistic compares the full model with a null model with all fixed effects deleted (except typically the intercept) while retaining exactly the same covariance structure.

Furthermore, the R2 statistic leads immediately to a natural definition of a partial R2 statistic. A mixed model in which ethnicity gives a very small p-value as a longitudinal predictor of blood pressure (BP) compellingly illustrates the value of the statistic.

In sharp contrast to the extreme p-value, a very small R^2 , a measure of statistical and scientific importance, indicates that ethnicity has an almost negligible association with the repeated BP outcomes for the study.

Leave-One-Out Diagnostics with `lmeU`

Galecki et al discuss the matter of LME influence diagnostics in their book, although not into great detail.

The command `lmeU` fits a model with a particular subject removed. The identifier of the subject to be removed is passed as the only argument

A plot ofthe per-observation diagnostics individual subject log-likelihood contributions can be rendered.

Likelihood Displacement

$$LD(\boldsymbol{\omega} = 2[L\hat{\boldsymbol{theta}} - \hat{\boldsymbol{theta}}_{\boldsymbol{\omega}}$$

Large values indicate that $\hat{\boldsymbol{theta}}$ and $\hat{\boldsymbol{theta}}_{\boldsymbol{\omega}}$ differ considerably.

7 Likelihood Distance

The likelihood distance gives the amount by which the log-likelihood of the full data changes if one were to evaluate it at the reduced-data estimates. The important point is that $l(\psi_{(U)})$ is not the log-likelihood obtained by fitting the model to the reduced data set.

It is obtained by evaluating the likelihood function based on the full data set (containing all n observations) at the reduced-data estimates.

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ψ that were subject to updating.

7.1 Likelihood Distance

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ϕ that were subject to updating.

8 Likelihood Distance

The likelihood distance gives the amount by which the log-likelihood of the full data changes if one were to evaluate it at the reduced-data estimates. The important point is that $l(\psi_{(U)})$ is not the log-likelihood obtained by fitting the model to the reduced data set.

It is obtained by evaluating the likelihood function based on the full data set (containing all n observations) at the reduced-data estimates.

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ψ that were subject to updating.

8.1 Likelihood Distance

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ϕ that were subject to updating.

9 Likelihood Distance

The likelihood distance gives the amount by which the log-likelihood of the full data changes if one were to evaluate it at the reduced-data estimates. The important point is that $l(\psi_{(U)})$ is not the log-likelihood obtained by fitting the model to the reduced data set.

It is obtained by evaluating the likelihood function based on the full data set (containing all n observations) at the reduced-data estimates.

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ψ that were subject to updating.

9.1 Likelihood Distance

The likelihood distance is a global, summary measure, expressing the joint influence of the observations in the set U on all parameters in ϕ that were subject to updating.

Missing Data in Method Comparison Studies

The matter of missing data has not been commonly encountered in either Method Comparison Studies or Linear Mixed Effects Modelling. However Roy (2009) deals with the relevant assumptions regrading missing data.

Galecki & Burzykowski (2013) tackles the subject of missing data in LME Modelling.

Furthermore the nlmeU package includes the `patMiss` function, which "allows to compactly present pattern of missing data in a given vector/matrix/data frame or combination of thereof".