Likelihood-based Inference for Mixed-Effects Models with Censored Response Using the Multivariate-t Distribution

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Abstract: Mixed-effects models are commonly used to fit longitudinal or repeated measures data. A complication arises when the response is censored, for example, due to limits of quantification of the assay used. Although the normal distributions are commonly assumed for the random effects and the residual errors, such assumptions make inferences vulnerable in the presence of outliers. The sensitivity to outliers and the need of heavy tailed distributions for random effects and residual errors motivate us to develop a likelihood-based inference for linear and nonlinear mixed effects models with censored response (NLMEC/LMEC) based on the multivariate Student-t distribution. An ECM algorithm is developed for computing the maximum likelihood estimates for NLMEC/LMEC with the standard errors of the fixed effects and the exact likelihood value as a by-product. The algorithm uses the closed-form expressions at the E-step, which relies on the formulas of the mean and variance of a truncated multivariate-t distribution. The proposed algorithm is implemented in the R package \textit{tlme}. The proposed methodology is applied to analyze longitudinal HIV viral load data in the two recent AIDS studies. In addition, a simulation study is conducted to examine the performance of the proposed method and carry out the comparison with the approach by \textit{?}.

Key words and phrases: Censored data, HIV viral load, ECM Algorithm, influential observations, mixed-effects models, outliers.