

Likelihood-based Inference for Mixed-Effects Models with Censored Response Using Skew-Normal 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 normal distributions are commonly assumed for random effects, such assumption may be unrealistic obscuring important features of among-individual variation. We relax this assumption by consider a likelihood-based inference for linear and nonlinear mixed effects models with censored response (NLMEC/LMEC) based on the multivariate skew-normal 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 closed-form expressions at the E-step, that rely on formulas for the mean and variance of a truncated multivariate skew-normal distribution. The proposed algorithm is implemented in the R package `skewlme`. It is applied to analyze longitudinal HIV viral load data in two recent AIDS studies. In addition, a simulation study is conducted to examine the performance of the proposed methods.