

Title:

**Flexible Modeling of Fixed and Random Effects in Generalized Mixed Models for Longitudinal Data**

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Abstract:

To circumvent the computational complexity of likelihood inference in generalized mixed models that assume linear or more general additive regression models of covariate effects, Laplace's approximations to multiple integrals in the likelihood have been commonly used without addressing the issue of adequacy of the approximations for individuals with sparse observations. In this paper, we propose a hybrid estimation scheme to address this issue. The likelihoods for subjects with sparse observations use Monte Carlo approximations involving importance sampling, while Laplace's approximation is used for the likelihoods of other subjects that satisfy a certain diagnostic check on the adequacy of Laplace's approximation. Because of its computational tractability, the proposed approach allows flexible modeling of covariate effects by using regression splines and model selection procedures for knot and variable selection. Its computational and statistical advantages are illustrated by simulation and by application to longitudinal data from a fecundity study of fruit flies.