

## Local Influence in Two-treatment Balanced Cross-over Designs

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The aim of influence analysis is to develop methods to detect influential observations without re-estimating the model. However, this task gets complicated when applying mixed linear models, mainly because the maximum likelihood estimators (MLEs) of mean and variance parameters depend on each other. In this article, we propose a methodology to detect influential observations in the context of cross-over design models with random individual effects. Existence of explicit MLEs of mean and variance parameters in mixed linear models with treatment, carry-over, period and sequence effects is proven. It is emphasized that perturbations, which are used for studying "influence", should be performed under the restriction that MLEs remain explicit in the perturbed model. Two influence functions, the delta-beta influence and variance-ratio influence, are tools to evaluate the influence on the estimates of mean and variance parameters, respectively, with respect to the used case-weighted perturbations. In the suggested approach, the expressions of the delta-beta and variance-ratio influences for a two-treatment cross-over design are derived. The influence quantities of each parameter turn out to be closed-form functions of orthogonal projections of residuals in the unperturbed model.

**Key Words:** Influential observation, explicit maximum likelihood estimate, mixed linear model, perturbation scheme