Flexible modeling of the error and/or random effect structure in linear mixed models and survival models with medical applications

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Abstract

In the first part of the talk, a linear mixed model with a smooth random effects density is proposed. Assuming a more flexible distribution for the random effects is of importance to better estimate the random effects and when dealing with missing data. The approach is related to P-spline smoothing of Eilers and Marx (1996) to yield a more flexible estimate of the random effects density. However, the approach differs from theirs in that the B-spline basis functions are replaced by approximating Gaussian densities (which are their limiting forms). Fitting the model involves maximizing a penalized marginal likelihood. The best penalty parameter minimizes Akaike's Information Criterion employing Gray's results (1992). Although the method is applicable to any dimensions of the random effects structure, in this paper the two-dimensional case is explored. The methodology is conceptually simple, and it is easy to fit in practice. This approach is applied to the cholesterol data first analyzed by Zhang and Davidian (2001) and to dental data of the Signal Tandmobiel study. A simulation study shows that the approach yields almost unbiased estimates of the regression and the smoothing parameters in small sample settings. Consistency of the estimates can be shown in a particular case.

The above approach can also be applied in a variety of other models. In the second part of the talk we will examine its usefulness to fit accelerated failure time models with a flexible error distribution. The method allows left-, right- and interval censoring. It will be shown that our approach comes close to a non-parametric approach and can be useful when a mix of types of censoring is present in the data. Finally, the method can also be applied to fit bivariate survival models. As a by-product the method allows easier computation of Kendall’s tau, again when left-, right or interval censoring is present. Both survival approaches will be applied to dental data from the Signal Tandmobiel Study and their small sample performance will be illustrated with simulation studies.