Optimum designs for enzyme kinetic models with co-variates

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Abstract

In this talk we consider a population optimum design of experiments for non-linear models and in the specific application to enzyme kinetic studies.

In the early stage of drug development pharmaceutical companies are interested in whether the new candidate medicinal product interacts with other drugs. Since most of the drugs are metabolized in human liver, these early stage pharmacokinetic experiments are conducted at different levels of concentration of the new compound applied to liver tissues representing "subjects" in the study. Also, the liver tissues differ in some systematic way what can be incorporated in the model as a function of co-variates. In our studies, which are based on a set of real data, we find that some of the parameters of this function differ across the population and so are treated as random. The question is about the choice of the liver tissues as well as the levels of concentration of the new medicinal product so that all the model parameters are estimated with high precision. Although it is set in a specific application it prompts several methodology questions in the optimum design theory to be answered.

Keywords

Mixed-effects model, D-optimality, Transform-both-sides model.