Experiments for enzyme kinetic models

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Abstract

The presence of an inhibitor in enzyme kinetic reactions leads to a number of potential nonlinear generalizations of the Michaelis-Menten model, depending on the particular mechanism of inhibition. The talk will present analytical expressions for the D-optimum designs for the parameters of four extended models, all nonlinear. These analytical expressions are not only important in themselves but greatly facilitate the study of design robustness: the efficiency of a proposed design can readily be established over a wide range of parameter values and the variation of the design with the parameters can be exhibited. A design robust to incorrect assumptions about the parameters can then be chosen in the light of this information.

Designs for subsets of the parameters are of interest when trying to establish the mechanism of inhibition and hence the appropriate model. It does not seem to be possible to find analytical expressions for such D_S-optimum designs. However numerical studies indicate that designs on the support points of the D-optimum designs, although with different weights, are often highly efficient.

In some cases the reduction to a simpler model occurs when two parameters have equal values. Then it is possible to rewrite the models so that parameter equality is equivalent to a new parameter being equal to zero. A D_S-optimum design can then be found for estimating this parameter as precisely as possible, leading to a powerful test of the hypothesis of parameter equality. An alterative is to use a T-optimum design for discriminating between the model in which the parameters are set equal and that in which they are not. Although the two approaches are identical for linear models, they are not so for nonlinear models. The two design approaches will be compared and the extent to which they differ elucidated.

It is intended that several of the theoretical points will be illustrated with experimental examples from the pharmaceutical industry.