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Optimal discrimination designs for exponential regression models

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Abstract

We investigate optimal designs for discriminating between exponential regression models of different complexity, which are widely used in the biological sciences; see, e.g., Landaw [1995. Robust sampling designs for compartmental models under large prior eigenvalue uncertainties. Math. Comput. Biomed. Appl. 181–187] or Gibaldi and Perrier [1982. Pharmacokinetics. Marcel Dekker, New York]. We discuss different approaches for the construction of appropriate optimality criteria, and find sharper upper bounds on the number of support points of locally optimal discrimination designs than those given by Caratheodory's Theorem. These results greatly facilitate the numerical construction of optimal designs. Various examples of optimal designs are then presented and compared to different other designs. Moreover, to protect the experiment against misspecifications of the nonlinear model parameters, we adapt the design criteria such that the resulting designs are robust with respect to such misspecifications and, again, provide several examples, which demonstrate the advantages of our approach.

MSC: 62K05; 62J02

Keywords: Compartmental model; Model discrimination; Discrimination design; Locally optimal design; Robust optimal design; Maximin optimal design

1. Introduction

In the biological and chemical sciences, the expected response of an experiment at some experimental condition x is commonly modeled as a function in x depending nonlinearly on some unknown parameters. An important class within the nonlinear regression models are exponential models of the form

$$\eta_k(x,\theta)=\sum_{i=1}^{k} a_i \mathrm{e}^{-\lambda_i x}, \quad k \geqslant 1, \quad x \in [0,\infty), \tag{1}$$

which have applications in chemical kinetics (see Gibaldi and Perrier, 1982) (in particular toxicokinetic experiments (see Becka et al. (1992, 1993)) or microbiology (see Alvarez et al., 2003, who used a model of type (1) to describe *Escherichia coli* inactivation by pulsed electric fields). Landaw (1985) fitted an exponential model to describe open,

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noncyclic k-compartmental systems. Since statistical inference can be improved considerably by choosing appropriate experimental conditions, at which the observations are taken, the class of models (1) has been considered in a few articles on optimal design of experiment (see Ermakov and Melas, 1995; Dette et al., 2006a,b; where the properties of D-, c- and E-optimal designs are investigated).

In most articles on optimal design, the authors assume that the model under consideration is already known except for the values of the unknown parameters, thus dealing with optimality criteria that are efficient for parameter estimation within a fixed model. In many applications, however, the form of the regression function will not be known exactly, i.e., the experimenter will have to decide among a set of competing classes of functions, which of them describes the data most adequately. The design problem for discrimination between competing nonlinear models has found much less attention in the literature than problems for parameter estimation (see, e.g., Atkinson and Fedorov, 1975a,b or Dette et al., 2005). For linear models, optimal designs for model discrimination have been discussed by several authors; see, e.g., Srivastava (1975, 1977), who mainly considered applications to 2^m factorial experiments. Stigler (1971) and Studden (1982) investigated designs which are on the one hand efficient for estimating the parameters in a given polynomial regression model and on the other hand allow to test this model against a polynomial of higher degree. Läuter (1974) proposed designs which are optimal for a given class of models, and this approach was successfully applied by Dette (1990, 1994), Zen and Tsai (2002) and Tsai and Zen (2004) to the class of polynomial models and by Zen and Tsai (2004) to the class of trigonometric regression models.

The goal of this article is to find designs that are efficient for discriminating between models of form (1) where the value of k, i.e., the number of exponential terms contributing to the model, is not fixed in advance. If for example a small model (small k) proves to be appropriate the number of parameters to be estimated will also be small so that estimation will be more efficient. Thus, either experimental costs can be reduced without losing precision in estimation by carrying out less runs, or the precision of the estimation will increase (for a fixed number of runs).

Since optimal designs with respect to classical optimality criteria such as the D-criterion depend on the nonlinear model parameters they are termed "locally" optimal. For model (1), the optimal discrimination designs will therefore depend on the value of $\lambda = (\lambda_1, \ldots, \lambda_k)$. Application of these designs can therefore only be efficient if a good guess for λ is available. Locally optimal designs, however, provide a basis for the construction of designs, which are more robust with respect to misspecifications of the nonlinear parameters, such as Bayesian or maximin optimal designs, which will be discussed later on.

The article at hand is organized as follows. Section 2 proposes several different optimality criteria that are suitable for finding discrimination designs for models of form (1) with different degrees. In Section 3, we present some analytical results, which facilitate the numerical construction of locally optimal designs substantially. In particular, we derive explicit bounds on the number of support points of the locally optimal designs with respect to the optimality criteria discussed in Section 2. Various examples of optimal designs are displayed in Section 4, where we also investigate their performance compared to different uniform designs and designs, which are optimal for parameter estimation in the largest model. Furthermore, emphasis in this section will be on robust designs with respect to misspecifications of the unknown parameters and their performance. For this purpose we determine maximin optimal designs, and compare their performance with the locally optimal designs. The proofs of our results, finally, are deferred to an appendix.

2. Optimality criteria

We consider an experiment with N independent observations Y_i, $i = 1, \ldots, N$, at experimental conditions x_i, which are modeled by

$$Y_i = \eta_k(x_i, \theta) + \varepsilon_i, \quad i = 1, \ldots, N, \tag{2}$$

where the errors ε_i are assumed i.i.d. with zero expectation and finite common variance, and the regression function $\eta_k(x, \theta)$ is of form (1) for some parameter $k \geqslant 1$. By θ we will denote the vector of unknown parameters in (1), i.e., $\theta = (a_1, \lambda_1, \ldots, a_k, \lambda_k)^{\mathrm{T}}$. Without loss of generality we assume that $a_j \neq 0$, $\lambda_j > 0$ and $\lambda_j \neq \lambda_i$ for $j \neq i$, $i, j = 1, \ldots, k$.

An approximate design

$$\xi = \begin{pmatrix} x_1 & \ldots & x_n \\ w_1 & \ldots & w_n \end{pmatrix}$$