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JOURNAL OF THE INDIAN SOCIETY OF AGRICULTURAL STATISTICS 72(1) 2018 27–32

D-Optimal Designs for Exponential and Poisson Regression Models

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Received 01 November 2017; Revised 29 December 2017; Accepted 30 December 2017

SUMMARY

In the present study, the class of nonlinear models, with intrinsically linearly related mean response and input variables, were explored for the generation of locally D-optimal designs. It has been found that these models have the advantage of design construction in transformed or coded design space with suitable transformation in initial parameter guesses. Exponential and Poisson regression models with two continuous input variables were investigated. For the construction of D-optimal designs, the modified version of Fedorov algorithm was used that require a suitable candidate set representing the design space along with the initial parameter guesses. The efficient method of constructing the candidate sets with respect to each model is proposed. The optimality of generated designs was validated using general equivalence theorem.

Keywords: Candidate set, D-optimality, Fisher information matrix, General equivalence theorem, Modified Fedorov exchange algorithm, Standardized variance function.

1. INTRODUCTION

Nonlinear models are unavoidable in many agricultural and industrial situations. These models are formulated either based on firm theoretical results or analysis of previously available data. Thus, under such situations if an experiment has to be conducted, the experimental design should incorporate nonlinear component also. Violating the assumption of linearity in the model might pose problems in design construction, namely dependency of design on initial parameter guesses and computational intensive design construction procedure. Though dependency on initial parameter guesses are unavoidable as emphasized by Palanichamy (1993), we found that for certain nonlinear models it is possible to generate designs in favourable range of design variables by transforming the initial parameter guesses given for original design variables range. The design construction procedure becomes computationally more difficult for the cases of experiments with continuous input variables.

Chernoff (1953) was probably the first to address the issue of developing designs for nonlinear models and discussed the use of initial parameter guesses. Designs depending on initial parameter guesses are called local. Logistic model has been extensively studied for the construction of optimal designs. But most of the literature focuses on one variable cases [See Ford *et al.* (1992), Sebastiani and Settini (1997), Mathew and Sinha (2001), Woods *et al.* (2006), Dror and Steinberg (2006) and Li and Majumdar (2008)]. Wang *et al.* (2006) and Russell *et al.* (2009) studied Poisson regression model and constructed D−optimal designs. Lall *et al.* (2018) constructed D-optimal saturated designs for logistic model through algorithmic approach.

In the present paper, locally D-optimal designs for exponential and Poisson regression models with two continuous variables have been obtained by transforming initial parameter guesses for design generation under transformed or rescaled input variables range. This approach can only be followed under nonlinear models with intrinsically linear mean response and input relationship. The issue of construction of candidate sets for implementing the

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modified version of Fedorov algorithm is addressed Under different model settings, the efficient method of constructing a candidate set for successful performance of the algorithm is given. We investigate exponential and Poisson regression models and obtained D-optimal designs under these model setups.

2. MODEL AND ALGORITHMIC PROCEDURE

A nonlinear model with intrinsically linear mean response and input relation can be defined as:

$$E(y_u) = \eta(\mathbf{x}_u, \boldsymbol{\theta}), \; u = 1, 2, \ldots, n \qquad (1)$$

where, y_u is the response, $\mathbf{x}_u$ is the input setting, $\boldsymbol{\theta}$ is the vector of unknown parameters and $\eta(\mathbf{x}_u, \boldsymbol{\theta})$ is the intrinsically linear relationship between mean response and input variables. This relational function is called intrinsically linear because it can be transformed to a linear function. Following Atkinson *et al.* (2007), the basic notations and terms are defined here.

For model (1), a Fisher Information Matrix (FIM) of a design say ξ with n design points can be defined as:

$$\mathbf{M}(\xi, \boldsymbol{\theta}) = \frac{1}{n} \sum_{x} \left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right] \left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right]' \qquad (2)$$

A D-optimal design maximizes the determinant of its respective FIM compared to any other design for a given number of runs. For a given design ξ, standardized variance function is defined for any point $\mathbf{x}$ from the design space (χ) as:

$$d(\xi, \mathbf{x}) = \left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}'} \right] \mathbf{M}^{-1}(\xi, \boldsymbol{\theta}) \left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right] \qquad (3)$$

Let $\boldsymbol{\theta}_0$ be the initial parameter guess. As $\eta(\mathbf{x}, \boldsymbol{\theta})$ is nonlinear, both FIM and standardized variance function will depend upon $\boldsymbol{\theta}_0$. Thus a D-optimal design will also be dependent on $\boldsymbol{\theta}_0$. Optimality of a given design can be checked using General Equivalence theorem which was extended to nonlinear models by White (1973) and Whittle (1973). For a D-optimal design, the following inequality holds:

$$d(\mathbf{x}, \xi) = \left(\left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right]' \mathbf{M}^{-1}(\xi, \boldsymbol{\theta}) \left[\frac{\partial \eta(\mathbf{x}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right] \right)_{\boldsymbol{\theta} = \boldsymbol{\theta}_0} \le k \;, \; \forall \mathbf{x} \in \chi \qquad (4)$$

where, k is the number of unknown parameters in the model.

For construction of D-optimal designs for models with more than one continuous variable, we employ the Fedorov algorithm (Fedorov, 1972), which works on computation of design point exchange. The modified version of the algorithm used in this study is as follows:

(i) Obtaining Candidate Set (CS): A grid of design points representing the design space.

(ii) Selecting Initial design (ξ_0): A random or user provided design of size n with positive determinant of its FIM.

(iii) Use of an exchange computation: one design point is exchanged between the design and the candidate set at every iteration until the stopping criterion is met.

(iv) Stopping criterion: No significant improvement in determinant of FIM or the design satisfies the general equivalence theorem.

Let at iteration j, $\mathbf{x}_{in} \in$ Candidate Set, $\mathbf{x}_{out} \in$ design(j), $\mathbf{a} = \left. \frac{\partial \eta(\mathbf{x}_{out}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right|_{\boldsymbol{\theta} = \boldsymbol{\theta}_0}$ and $\mathbf{b} = \left. \frac{\partial \eta(\mathbf{x}_{in}, \boldsymbol{\theta})}{\partial \boldsymbol{\theta}} \right|_{\boldsymbol{\theta} = \boldsymbol{\theta}_0}$

Thus, the design point exchange can be performed by maximizing the following expression (Fedorov, 1972 page 100):

$$\Delta(x_{in}, x_{out}) = 1 + \mathbf{a}'\mathbf{N}_j^{-1}\mathbf{a} - \mathbf{b}'\mathbf{N}_j^{-1}\mathbf{b} - (\mathbf{a}'\mathbf{N}_j^{-1}\mathbf{a})(\mathbf{b}'\mathbf{N}_j^{-1}\mathbf{b}) + (\mathbf{a}'\mathbf{N}_j^{-1}\mathbf{b})^2 \qquad (5)$$

where, $\mathbf{N}_j = n \times \mathbf{M}(\xi_j, \boldsymbol{\theta})$.

Since a discrete representation of the design space is used here, it might be possible that some points other than candidate set can increase the determinant of FIM on performing exchange. Thus, optimality of design generated using Fedorov algorithm may not be guaranteed. To handle this problem, an additional search step is proposed. We assume that the design generated by the Fedorov algorithm is near to optimal design if not optimal and implement the above mentioned algorithm once again. This time the candidate set is reconstructed as the grid of design points in the vicinity of design (say ξ^{1*}), which was found using the original candidate set and the initial design is chosen as design ξ^{1*} only.

Let f($\mathbf{x}$, $\boldsymbol{\theta}$) be the linear polynomial function of $\mathbf{x}$ and $\boldsymbol{\theta}$ under nonlinear setup $\eta(\mathbf{x}, \boldsymbol{\theta})$ of model

(1). In model (1), the number of variables and their polynomial form is given by f(**x**, **θ**). Here, we have considered exponential and Poisson regression models for the following forms of f(**x**, **θ**) and obtained D-optimal designs:

$$f(\mathbf{x}, \boldsymbol{\theta}) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 \quad (6)$$

$$f(\mathbf{x}, \boldsymbol{\theta}) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_{12} x_1 x_2 \quad (7)$$

$$f(\mathbf{x}, \boldsymbol{\theta}) = \beta_0 + \beta_1 x_1 + \beta_{11} x_1^2 + \beta_2 x_2 + \beta_{22} x_2^2 + \beta_{12} x_1 x_2 \quad (8)$$

The maximum of standardized variance function give in (4) is denoted by by $\rho = \max_x d(\mathbf{x}, \xi)$.

3. TRANSFORMATION OF INITIAL PARAMETER GUESSES

In this paper, all the design input variables are rescaled to the range [-1, 1]. Thus, the initial parameter guesses provided by an expert or experimenter in context of original variables range, cannot be used directly in the design generation procedure. Let x_i, i = 1,2,...,v be a design variable in model (1), $x_i \in [a_i, b_i]$ and $z_i \in [-1, 1]$ be the corresponding rescaled or coded variable. From the theory of response surface methodology, it is known that $z_{iu} = \frac{(x_{iu} - x_{i0})}{\Delta_i}$, where, $x_{i0} = \{b_i + a_i\}/2$ and $\Delta_i = \{b_i - a_i\}/2$.

Since model (1) is intrinsically linear for mean response and input variables relation, we define

$$\eta(\mathbf{x}, \boldsymbol{\theta}) = g[f(\mathbf{x}, \boldsymbol{\theta})]$$

where, g() is some nonlinear function and f(**x**, **θ**) is as defined earlier. Let β_0, β_i and β_{ii} be the unknown parameters in model (1) with β_0 being intercept, β_i is coefficient of first order term corresponding to variable x_i and β_{ii} is the coefficient of second order or cross product term corresponding to x_i and x_i, where i = 1,2,...,v. Let α_0, α_i and α_{ii} be the parameters of the model corresponding to coded variables z_i. Then, $\alpha_0 = \beta_0 + \sum_{i=1}^{v} \beta_i x_{i0}$, $\alpha_i = \beta_i \Delta_i$ and $\alpha_{ii'} = \beta_{ii'} \Delta_i \Delta_{i'}$. This formulation is helpful in using a vector of initial parameter guesses with respect to original variables for generating designs in terms of coded variables.

4. CONSTRUCTION OF CANDIDATE SET

As discussed earlier, a candidate set is the discrete representation of continuous design space. The design generation can be seen as an optimization problem with the design criterion as objective function, candidate set as solution space and constraints related to variables and model. A candidate set should have low discrepancy or high uniform density. A candidate set with low density or high discrepancy might result in deletion of optimal and near optimal design points from the solution space. Although a candidate set with very high density seems tempting but it incurs huge computational costs at the same time. Evidently a candidate set with low density is bound to produce imprecise results. Hence, there is a trade off between accuracy and cost. There are two basic methods of constructing candidate set.

Method A: Let x_i, i = 1,2,...,v be a design variable in model (1) with $x_i \in [a_i, b_i]$ and S be the desired number of equidistant points in the range of any given design variable. The candidate points of variable x_i are given by $x_{is} = a_i + (b_i - a_i)s/S$, s = 0,1,...,S. Similarly for each variable S, candidate points are found and candidate set is constructed by simply taking the Cartesian product of set of candidate points for all variables. Thus, the total number of design points in candidate set for model (1) with v variables is $(S+1)^v$. In this study, $a_i = -1$ and $b_i = 1$, So, $x_{is} = -1 + 2s/S$.

Method B: It is similar to method A, except the candidate points for a given variable x_i is generated by taking equidistant points at a fixed increment (t) in its respective range. The total number of candidate points S for a variable x_i, $x_i \in [a_i, b_i]$ is given by $S = 1 + (b_i - a_i)/t$. Here $S = 1 + 2/t$.

Method A is more popular (Mandal and Torsney, 2006; Labadi and Wang, 2010) as it includes large fractions, while method B has candidate points with fixed size of fraction. In order to improve the Fedorov algorithm with candidate set constructed using method B, we propose an additional search step described below.

Let CS_0 be the candidate set generated using method B with increment t and Fedorov algorithm resulted in design ξ_0. Assuming ξ_0 is the design which lies in the neighbourhood of D-optimal design if it is not itself the D−optimal design, the following procedure is adopted for the case of two variables:

(i) Let d_{lm} be a point in design ξ_0, l = 1,2,...n and m = 1,2. For each d_{lm} generate r (say 21) equidistant points in the range $[d_{lm} - t, d_{lm} + t]$. Denote the set of r generated points by $\{d_{lm}\}$.

(ii) Take Cartesian product, $\{d_{l1}\} \otimes \{d_{l2}\} \forall l$ and combine the resulting l grids into a single grid of points. The result is a grid with structure of a data frame or matrix with dimension $lr^2 \times 2$.

(iii) Remove the design point or the row of grid found in step 2 with entry less than -1 or greater than +1.

The output is a grid in the vicinity of ξ_0. Using this grid as candidate set and the design as initial design one can easily reach towards D−optimal design. We found that incorporation of this additional step gives improved results as compared to method A. The candidate points generated by method A are not equidistant and hence applying modification to this method will not give complete coverage of the design space.

5. EXPONENTIAL MODEL

The exponential model is one of the most popular nonlinear models in agricultural and industrial situations. The general form of this model in our framework is defined as follows:

$$y_u = \exp[f(\mathbf{x}_u, \boldsymbol{\theta})] + e_u, \quad u = 1, 2, \ldots, n \tag{9}$$

where, y_u is the response corresponding to i^{th} design point and $e_u \sim N(0, \sigma^2)$, $\sigma^2 > 0$ is the error.

For a design ξ with n design points under exponential model setup and $\boldsymbol{\theta}_0$ being the vector of initial parameter guesses, FIM can be given by:

$$\mathbf{M}(\xi, \boldsymbol{\theta}) = \frac{1}{n} \sum_{u=1}^{n} e^{2f(\mathbf{x}, \boldsymbol{\theta}_0)} \mathbf{f}(\mathbf{x})\mathbf{f}(\mathbf{x})' \tag{10}$$

where, $\mathbf{f}(\mathbf{x})$ is such that $f(\mathbf{x}, \boldsymbol{\theta}) = \mathbf{f}(\mathbf{x})'\boldsymbol{\theta}$.

For two variables under first and second order polynomial form of $f(\mathbf{x}, \boldsymbol{\theta})$, D-optimal designs have been generated and reported in Table 1, 2 and 3. The tables report the design generated for a model with given initial parameter guesses using the methods A and B for construction of candidate set (CS). The method A was constructed by taking Cartesian product of the sets of S +1 candidate points for the two variables x_1 and x_2. In the same line, method B was used to obtain the candidate set by using S candidate

Table 1. First order exponential model with two variables

CS	S	Design with θ_0 = [4, 1.5, 1.5]′				$\lvert M(\xi, \theta)\rvert$	ρ
A	**19**	x_1	**1**	**1**	**0.368421**	**2.32E+14**	**3.009732**
		x_2	**1**	**0.368421**	**1**		
	49	x_1	**1**	**1**	**0.346939**	**2.33E+14**	**3.001012**
		x_2	**1**	**0.346939**	**1**		
	99	x_1	**1**	**1**	**0.333333**	**1.93E+14**	**3**
		x_2	**1**	**0.333333**	**1**		
B	**21**	x_1	**1**	**1**	**0.33**	**2.33E+14**	**3**
		x_2	**1**	**0.33**	**1**		
	51	x_1	**1**	**1**	**0.332**	**2.33E+14**	**3**
		x_2	**1**	**0.332**	**1**		
	101	x_1	**1**	**1**	**0.334**	**2.33E+14**	**3**
		x_2	**1**	**0.334**	**1**		

Table 2. First order exponential model with two variables and interaction

CS	S	Design with θ_0 = [4, 1.5, 1.5, 0.1]′					$\lvert M(\xi, \theta)\rvert$	ρ
A	19	x_1	1	0.368421	1	0.368421	1.10E+17	4.023282
		x_2	1	0.368421	0.368421	1		
	49	x_1	1	0.346939	1	0.346939	1.11E+17	4.002316
		x_2	1	0.346939	0.346939	1		
	99	x_1	1	0.333333	1	0.333333	1.11E+17	4.000185
		x_2	1	0.333333	0.333333	1		
B	21	x_1	1	0.33	1	0.34	1.11E+17	4
		x_2	1	0.33	0.34	1		
	51	x_1	1	0.336	1	0.336	1.11E+17	4.000001
		x_2	1	0.336	0.336	1		
	101	x_1	1	0.334	1	0.338	1.11E+17	4
		x_2	1	0.334	0.338	1		

Table 3. Second order exponential model with two variables and all second order terms

CS	S	Design with θ_0 = [4, 1.5, 1.5, 0.5, 0.5, 0.1]′							$\lvert M(\xi, \theta)\rvert$	ρ
A	19	x_1	-1	-1	0.789474	1	1	1	1.56E+30	6.04338
		x_2	-1	1	1	1	-1	0.368421		
	49	x_1	-1	-1	0.795918	1	1	1	1.57E+30	6.04232
		x_2	-1	1	1	1	-1	0.428571		
	99	x_1	-1	-1	0.777778	1	1	1	1.58E+30	6
		x_2	-1	1	1	1	-1	0.42		
B	21	x_1	-1	-1	0.776	1	1	1	1.58E+30	6
		x_2	-1	1	1	1	-1	0.42		
	51	x_1	-1	-1	0.776	1	1	1	1.58E+30	6
		x_2	-1	1	1	1	-1	0.42		
	101	x_1	-1	-1	0.778	1	1	1	1.58E+30	6
		x_2	-1	1	1	1	-1	0.42		

points taken for both the variables. For method B, the additional search step was also implemented to find the final designs reported in the tables. The number of runs in the designs is equal to the number of unknown parameters in the model. The tables also give the value of determinant of FIM for the respective designs along with the value of ρ to check their optimality.

6. POISSON REGRESSION MODEL

A Poisson regression model can be written as

$$Y_{ij} \sim \text{Poisson}(\lambda_i), \tag{11}$$

where $\lambda_i = \exp[f(\mathbf{x}, \boldsymbol{\theta})]$

In toxicity research, y_{ij} is the number of organisms or cells that survive the experiment for the j-th replicate at the i-th design point and we assume it follows a Poisson distribution with λ_i as the mean. Similar to exponential model the FIM is found as

$$\mathbf{M}(\xi,\boldsymbol{\theta}) = \frac{1}{n}\sum_{u=1}^{n} e^{f(\mathbf{x},\boldsymbol{\theta}_0)}\mathbf{f(x)f(x)'} \tag{12}$$

The difference in the form of FIMs of designs for exponential and Poisson regression model is due to the different response distributions. For details related to FIM see Atkinson *et al.* (2007), Wang *et al.* (2006) and Russell *et al.* (2009).

Table 4, 5 and 6 report the D-optimal designs found for different Poisson regression model setup.

Table 4. First order Poisson regression model with two variables

CS	S	Design with $\boldsymbol{\theta}_0$ = [4, 1.5, 1.5]′				$\lvert\mathbf{M}(\xi, \boldsymbol{\theta})\rvert$	ρ
A	19	x_1	1	-0.36842	1	2823620	3.002259
		x_2	1	1	-0.36842		
	49	x_1	1	-0.34694	1	2826881	3.000246
		x_2	1	1	-0.34694		
	99	x_1	1	1	-0.33333	2827466	3
		x_2	1	-0.33333	1		
B	21	x_1	1	-0.332	1	2827460	3
		x_2	1	1	-0.332		
	51	x_1	1	-0.336	1	2827443	3
		x_2	1	1	-0.336		
	101	x_1	1	-0.332	1	2827460	3
		x_2	1	1	-0.332		

According to the theoretical result given by Russell *et al.* (2009), the D-optimal design for first order Poisson regression model with two variables with initial parameter guesses $\boldsymbol{\theta}_0$ = [4, 1.5, 1.5]′will be {(1,1), (1,-1/3),(-1/3,1)}.

Table 5. First order Poisson regression model with two variables and interaction

CS	S	Design with $\boldsymbol{\theta}_0$ = [4, 1.5, 1.5, 0.1]					$\lvert\mathbf{M}(\xi, \boldsymbol{\theta})\rvert$	ρ
A	19	x_1	1	-0.36842	-0.36842	1	18954381	4.004941
		x_2	1	-0.36842	1	-0.36842		
	49	x_1	1	-0.34694	-0.30612	1	19006831	4.000793
		x_2	1	-0.34694	1	-0.30612		
	99	x_1	1	-0.33333	-0.33333	1	19014712	4.000185
		x_2	1	-0.33333	1	-0.33333		
B	21	x_1	1	-0.34	-0.324	1	19016296	4
		x_2	1	-0.34	1	-0.324		
	51	x_1	1	-0.336	-0.328	1	19016318	4
		x_2	1	-0.336	1	-0.328		
	101	x_1	1	-0.34	-0.328	1	19016037	4
		x_2	1	-0.34	1	-0.328		

Table 6. Second order Poisson regression with two variables and all second order terms

CS	S	Design with $\boldsymbol{\theta}_0$ = [4, 1.5, 1.5, 0.5, 0.5, 0.1]′							$\lvert\mathbf{M}(\xi, \boldsymbol{\theta})\rvert$	ρ
A	19	x_1	-1	-1	1	1	0.578947	1	4.62E+13	6.013574
		x_2	-1	1	-1	1	1	0.157895		
	49	x_1	-1	-1	1	1	0.55102	1	4.63E+13	6.003134
		x_2	-1	1	-1	1	1	0.183674		
	99	x_1	-1	-1	1	1	0.555556	1	4.63E+13	6.000997
		x_2	-1	1	-1	1	1	0.191919		
B	21	x_1	-1	-1	1	1	0.56	1	4.63E+13	6
		x_2	-1	1	-1	1	1	0.192		
	51	x_1	-1	-1	1	1	0.56	1	4.63E+13	6
		x_2	-1	1	-1	1	1	0.192		
	101	x_1	-1	-1	1	1	0.56	1	4.63E+13	6
		x_2	-1	1	-1	1	1	0.192		

7. DISCUSSION

The choice of nonlinear models with intrinsically linear mean response and input variable relation in the present study helped in generating designs in desired coded variable range. This type of consideration is not needed for linear models as the designs, FIMs and other functions do not depend upon the initial parameter guesses. Since the initial parameter guesses are obtained from either previously available data or expert opinion, it is reasonable to expect the guesses according to original design variables range. A working formula for suitable transformation of the initial parameter guesses has been given for design generation in coded design variable space. For searching the designs we implemented the modified version of Fedorov algorithm for nonlinear models with two continuous input variables. As this algorithm was originally devised for discrete design space, applying it for continuous design space require high computational resources. We undertook the study of efficient construction of candidate set under different model setups. Candidate set construction method A was found to work with fair accuracy for 99 candidate points in each variable. On the other hand, method B coupled with our proposed additional step was found to perform better than method A. Method B is recommended for construction of candidate set with an increment of 0.1 or 21 candidate points in each variable for the model setups considered in this study. The D-optimal designs for exponential and Poisson regression model were generated. The reported designs were validated for optimality by empirically computing the inequality given by general equivalence theorem. If proper transformation of initial parameter guesses is not available then the reported procedure can be easily customized for original variables range. All computations presented here were performed by developing suitable R-codes available with the authors.

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