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WHEN IS AN EQUALLY-WEIGHTED DESIGN D-OPTIMAL?

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Abstract. We discuss conditions under which an equally weighted design is D-optimal. The concept of a model being maximally invariant with respect to a set is introduced and is shown to be useful in this work. Several illustrative examples are given, including two biomedical applications using compartmental and segmented models.

Key words and phrases: D-optimum design, equivalence theorem, G-optimum design, information matrix.

1. Introduction

Designs which are equally supported over a set of equally spaced points are commonly called uniform designs. They are popular because such designs are easy to construct and enjoy some optimality properties, see Wiens (1991) for example. These designs are also frequently used when there are no clear alternatives. However, uniform designs have their limitations and some of their disadvantages are noted in Wong (1996) and Eastwood (1996). For instance, in dose response studies, there may be ethical concern over assigning equal numbers of patients to all dosage levels, especially the highest and lowest or 'no treatment' dosage levels, since such levels may carry extra risk for patients. Modification of these designs can include unbalancing the design to permit unequal spacing for the dosage levels or else unequal weights at the different dosage levels. The aim is to retain as much of the appeal of the uniform design as possible and at the same time provide some flexibility to the researcher.

In this work, we consider equally weighted designs but permit the design points to be unequally spread over the design space. Interest in such designs arises

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primarily from the observation that many popular designs, like D-optimal designs, are frequently equally weighted but otherwise are not necessarily uniformly spaced. In addition, recent work suggests optimal designs for many complex models are also equally weighted. For example, the Bayesian D-optimal designs found by Dette and Wong (1996, 1998) for estimating the parameters in a polynomial model when there is vague information on the heteroscedasticity are equally weighted.

The statistical background is in Section 2 whilst the concept of a model being maximally invariant with respect to a set is given in Section 3, along with our main results. Examples are provided in Section 4 and Section 5 contains a discussion of our results.

2. Background

Consider the linear regression model,

$$E[y(x)] = \theta^t f(x) = \theta_1 f_1(x) + \cdots + \theta_p f_p(x), \qquad x \in X, \tag{2.1}$$

where $f(x)$ is a vector consisting of p known continuous and linearly independent functions on a given compact set X, θ is a vector consisting of p unknown constants and the variance of y is $\text{var}[y(x)] = w^{-1}(x)$. Here $w(x)$ is a known weight function and is usually called the efficiency function in the design literature.

A probability measure, ξ, on X which is supported by a finite set, is an (approximate) design. This means if the design ξ has mass $\xi(x_i)$ at x_i, $i = 1, 2, \ldots, k$ and a total of n observations is to be taken from the experiment, then approximately $n\xi(x_i)$ observations are taken at x_i, $i = 1, \ldots, k$.

Following convention, the standardized information matrix for the design ξ is

$$M(\xi) = \sum_{x \in X} f(x) f^t(x) w(x) \xi(x).$$

The D- and G-optimum criteria are defined by

$$\Phi_D[M(\xi)] = -\log\det M(\xi), \qquad \Phi_G[M(\xi)] = \max_{x \in X} f^t(x) M^{-1}(\xi) f(x).$$

A design which minimizes these functions is called a D- or G-optimal design. These criteria are related in the following way (Kiefer and Wolfowitz (1960)): If $w(x) = 1$, the following statements are equivalent:

a) ξ is the D-optimum design,

b) ξ is the G-optimum design,

c) The following inequality is verified:

$$p \geq f^t(x) M^{-1}(\xi) f(x), \tag{2.2}$$

with equality at the support points of ξ.

Part (c) provides a convenient way for checking graphically whether a given design, ξ, is D-optimal. Further details of this setup are given in Fedorov (1972) and, Atkinson and Donev (1992).

In the next section, we develop a systematic way of determining if an equally weighted design is D-optimal. In the process, sufficient conditions are given. Although these conditions are derived from the equivalence theorem of Kiefer and Wolfowitz (1960), we find the alternative formulation given here useful. This is because it focusses on equally-weighted designs and these designs are very popular among practitioners. Additionally, our examples in Section 4 show these conditions are easy to check in practice.

3. A Maximal Invariant Condition (MIC)

In order to facilitate computation, we assume that $w(x) = 1$, $x \in X$; otherwise since $w(x)$ is known, we can reparameterize the model to acheive this. Thus there is no loss of generality in our results provided the maximal invariant condition given below holds. Suppose that the support design is $X_\xi = \{x_1, \ldots, x_p\}$. Writing $a_{ik} = f_i(x_k)\xi(x_k)$ and $b_{jk} = f_j(x_k)$, and denoting $A = (a_{ik})$ and $B = (b_{jk})$, we have

$$\det M(\xi) = \det A \det B = \prod_{k=1}^{p} \xi(x_k) \det[f_i(x_k)]^2. \tag{3.1}$$

In the general case when $X_\xi = \{x_1, \ldots, x_r\}$ with $r \geq p$, we have

$$\begin{aligned} \det M(\xi) &= \det \left[\left\{ \sum_{k=1}^{r} f_i(x_k) f_j(x_k) \xi(x_k) \right\} \right] \\ &= \sum_{k_1 < \cdots < k_p} \xi(x_{k_1}) \cdots \xi(x_{k_p}) \det[\{f_i(x_{k_j})\}]^2, \end{aligned} \tag{3.2}$$

where the summation is taken over all ordered subsets of size p from $\{1, 2, \ldots, r\}$. Since the function $\psi(x_1, \ldots, x_p) = \det[\{f_i(x_j)\}]^2$ is continuous on the compact set X^p, its extremes are reached on X^p. From (3.2), it appears convenient to consider only the points where the maximum of the function ψ is reached. However, it is possible that the function ψ reaches its maximum at the points $(x_1, \ldots, x_p)$ and $(x'_1, \ldots, x'_p)$, but this maximum is not reached, for example, at the point $(x_1, \ldots, x_{p-1}, x'_p)$. This is problematic because the determinant of the standardized information matrix depends on the value of the function ψ at every p-tuple formed by points from X_ξ.

For these reasons we assume the following hypothesis:

MAXIMAL INVARIANT CONDITION (MIC): The model (2.1) satisfies the maximal invariant condition if, and only if, there exists a maximal set of points $\{z_1, \ldots, z_r\}$ in X, such that

$$\psi(z_{\nu(1)}, \ldots, z_{\nu(p)}) = \max\{\psi(x_1, \ldots, x_p) \mid (x_1, \ldots, x_p) \in X^p\},$$

for every injective map $\nu : \{1, \ldots, p\} \to \{1, \ldots, r\}$. The set $\{z_1, \ldots, z_r\}$ is called the maximal invariant set.

Notice that the function ψ is symmetric in the sense that for every permutation τ,

$$\psi(x_1,\ldots,x_p)=\psi(x_{\tau(1)},\ldots,x_{\tau(p)}).$$

Therefore if the maximum is reached at a point $(x_1,\ldots,x_p)$, then it is also reached at the point $(x_{\tau(1)},\ldots,x_{\tau(p)})$. Clearly, when $r=p$, the MIC holds automatically.

PROPOSITION 1. *If the model* (2.1) *satisfies the MIC, any D-optimal design* ξ *supported on the set* $\{z_1,\ldots,z_r\}$ *is an equally weighted design. Furthermore, if* ξ *is the said design,*

$$\det M(\xi)=\frac{M}{r^p}\binom{r}{p},$$

where $M=\max\{\psi(x_1,\ldots,x_p):(x_1,\ldots,x_p)\in X^p\}$.

PROOF. Let $\alpha_i=\xi(z_i)$, $i=1,\ldots,r$. If the MIC holds,

$$\det M(\xi)=M\sum_{i_1<\cdots<i_p}\alpha_{i_1}\cdots\alpha_{i_p}.$$

The problem is summarized as follows:

$$\begin{cases}\max_{\alpha_1,\ldots,\alpha_r}\sum_{i_1<\cdots<i_p}\alpha_{i_1}\cdots\alpha_{i_p}\\ \text{subject to}\begin{cases}\alpha_i\geq 0, & i=1,\ldots,r\\ \sum_{i=1}^r\alpha_i=1.\end{cases}\end{cases}$$

Using Lagrange multipliers, the only solution is $\alpha_1=\cdots=\alpha_r=\frac{1}{r}$, which gives the maximum we are looking for and the determinant expression of the proposition.

PROPOSITION 2. *If the model* (2.1) *satisfies the MIC on the set* $\{z_1,\ldots,z_r\}$, *every design supported on r points or less is no better than the design of the last proposition. In addition,* $r\leq p(p+1)/2$.

PROOF. Let ξ be a design supported at $x_1,\ldots,x_k$ in X, $p\leq k\leq r$. By Proposition 1,

$$\begin{aligned}\det M(\xi)&=\sum_{i_1<\cdots<i_p}\psi(x_{i_1},\ldots,x_{i_p})\xi(x_{i_1})\cdots\xi(x_{i_p})\\ &\leq M\sum_{i_1<\cdots<i_p}\xi(x_{i_1})\cdots\xi(x_{i_p})\leq\frac{M}{k^p}\binom{k}{p}\leq\frac{M}{r^p}\binom{r}{p}.\end{aligned}$$

The last inequality is strict for $k<r$. Furthermore, the first inequality is strict whenever $\{z_1,\ldots,z_r\}\neq\{x_1,\ldots,x_k\}$. On the other hand if $r\geq p(p+1)/2$, there is another design with the same information matrix as ξ but with less than or equal to $p(p+1)/2$ support points; see Atkinson and Donev (1992), p. 96.

PROPOSITION 3. *Suppose* $\psi(x,y) = [f_1(x)f_2(y) - f_1(y)f_2(x)]^2$ *and* f_1 *and* f_2 *are differentiable functions on* $X = [a,b]$. *If the MIC is satisfied, then* $r = 2$.

PROOF. A maximum of ψ must be a maximum or a minimum of $\varphi(x,y) = f_1(x)f_2(y) - f_1(y)f_2(x)$. By the last part of Proposition 2, we can assume that the MIC holds with respect to a three point set $\{x_1, x_2, x_3\}$. The extremes of φ are either reached in the interior (derivatives zero) or on the boundary of X. It is easy to show that

$$\frac{f_1'(x_k)}{f_2'(x_k)} = \frac{f_1(x_j)}{f_2(x_j)} = \frac{f_1(x_i)}{f_2(x_i)}, \qquad \{i,j,k\} = \{1,2,3\}$$

unless $f_2(x_i) = 0$ or $f_2'(x_i) = 0$ or $f_1(x_i) = 0$ or $f_1'(x_i) = 0$, for some $i = 1,2,3$ which implies that φ vanishes at a pair of points. Let us assume now that $f_2(x_i) \neq 0$, $f_2'(x_i) \neq 0$, $f_1(x_i) \neq 0$, $f_1'(x_i) \neq 0$, for $i = 1,2,3$. If these three points are in the interior of X, then differentiating again implies that $\psi(x_i, x_j) = 0$. Therefore, at least one of the points must be a or b. Without loss of generality, suppose it is a. A similar argument for $\varphi(a,x)$ yields

$$\frac{f_1'(x_2)}{f_2'(x_2)} = \frac{f_1(a)}{f_2(a)} = \frac{f_1'(x_3)}{f_2'(x_3)} = \frac{f_1(x_2)}{f_2(x_2)},$$

which is again a contradiction. Thus, $r = 2$ and (x_1, x_2) is either an interior point or a boundary point of X.

THEOREM. a) *Suppose the model* (2.1) *satisfies the MIC and the maximal invariant set is* $\{z_1, \ldots, z_r\}$. *Then*

$$f^t(x)M^{-1}(\xi^\star)f(x) = \frac{p}{M\binom{r-1}{p-1}} \sum_{i_2<\cdots<i_p} \psi(x, z_{i_2}, \ldots, z_{i_p}), \qquad x \in X,$$

where $\xi^\star(z_1) = \cdots = \xi^\star(z_r) = 1/r$.

b) *In addition, if*

$$\max_{x\in X} \sum_{i_2<\cdots<i_p} \psi(x, z_{i_2}, \ldots, z_{i_p}) = M\binom{r-1}{p-1}, \tag{3.3}$$

the equally weighted design supported on the set $\{z_1, \ldots, z_r\}$ *is D-optimum.*

PROOF. The standardized information matrix of $\xi^\star$ is

$$M(\xi^\star) = \frac{1}{r}\sum_{i=1}^{r} f(z_i)f^t(z_i),$$

$$\det M(\xi^\star) = \sum_{i_1<\cdots<i_p} \psi(z_{i_1}, z_{i_2}, \ldots, z_{i_p})\xi^\star(z_{i_1})\cdots\xi^\star(z_{i_p}) = \frac{\binom{r}{p}}{r^p}M,$$

and

$$M^{-1}(\xi^\star) = \frac{r^p}{M\binom{r}{p}} \begin{pmatrix} M_{11}(\xi^\star) & \cdots & M_{1p}(\xi^\star) \\ \cdots & \cdots & \cdots \\ M_{p1}(\xi^\star) & \cdots & M_{pp}(\xi^\star) \end{pmatrix}.$$

Here,

$$\begin{aligned}
&(-1)^{i+j} r^{p-1} M_{ij}(\xi^\star) \\
&= \det \begin{pmatrix} \sum_{k=1}^r f_1^2(z_k) & \cdots & \sum_{k=1}^r f_1(z_k) f_p(z_k) \\ \cdots & \cdots & \cdots \\ \sum_{k=1}^r f_p(z_k) f_1(z_k) & \cdots & \sum_{k=1}^r f_p^2(z_k) \end{pmatrix}_{ij} \\
&= \sum_{i_2<\cdots<i_p} \det \begin{pmatrix} f_1^2(z_{i_2}) & \cdots & f_1(z_p) f_p(z_p) \\ \cdots & \cdots & \cdots \\ f_1(z_{i_p}) f_p(z_{i_p}) & \cdots & f_p^2(z_p) \end{pmatrix}_{ij} \\
&= \sum_{i_2<\cdots<i_p} \det \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_1(z_{i_p}) \\ \cdots & \cdots & \cdots \\ f_p(z_{i_2}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_i \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_p(z_{i_2}) \\ \cdots & \cdots & \cdots \\ f_1(z_{i_p}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_j,
\end{aligned}$$

where the subscript i or j outside the matrix means that row i or column j has been removed from the matrix. It follows that

$$\begin{aligned}
&f^t(x) M^{-1}(\xi^\star) f(x) \\
&= \frac{r^p}{M\binom{r}{p}} \left\{ \sum_{i=1}^p M_{ii}(\xi^\star) f_i^2(x) + 2 \sum_{i<j} M_{ij}(\xi^\star) f_i(x) f_j(x) \right\} \\
&= \frac{r^p}{M\binom{r}{p}} \frac{1}{r^{p-1}} \sum_{i_2<\cdots<i_p} \left\{ \sum_{i=1}^p f_i^2(x) \det \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_1(z_{i_p}) \\ \cdots & \cdots & \cdots \\ f_p(z_{i_2}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_i^2 \right. \\
&\quad + 2 \sum_{i<j} (-1)^{i+j} f_i(x) f_j(x) \\
&\quad \left. \cdot \det \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_1(z_{i_p}) \\ \cdots & \cdots & \cdots \\ f_p(z_{i_2}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_i \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_p(z_{i_2}) \\ \cdots & \cdots & \cdots \\ f_1(z_{i_p}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_j \right\} \\
&= \frac{p}{M\binom{r-1}{p-1}} \sum_{i_2<\cdots<i_p} \left\{ \sum_{i=1}^p (-1)^{i+1} f_i(x) \det \begin{pmatrix} f_1(z_{i_2}) & \cdots & f_1(z_{i_p}) \\ \cdots & \cdots & \cdots \\ f_p(z_{i_2}) & \cdots & f_p(z_{i_p}) \end{pmatrix}_i \right\}^2.
\end{aligned}$$

This completes the proof of part a). Part b) follows directly from part a) and (2.2).

The equivalence theorem is useful to check whether a design is D-optimal but it does not provide the optimal design. Our theorem provides an equally weighted D-optimal via the MIC and (3.3) if one exists. Verification of the MIC requires finding the maximum of a multi-dimensional real-valued function but verification of (3.3) requires finding the maximum of a univariate function only. In both cases, one can resort to any of the standard numerical recipes. Since (3.3) involves a function of one variable, usually a graphical check will suffice; Atkinson and Donev ((1992), Chapter 9) provides several illustrative examples.

4. Examples

We now apply the results in Section 3 to some known situations. These examples provide insights about the MIC and show it can be checked analytically in certain situations. Details of the calculation are straightforward and are omitted. In the first three examples, we have $r = p$ and in the fourth example, we have $r > p$. The fifth example shows that the points in the maximal invariant set can all be interior points of X. Note that when we have nonlinear models, the designs are locally D-optimal (Chernoff (1953)). This means the optimal designs depend on the nominal values of the parameters.

4.1 *Compartmental models*

These types of models are commonly used in pharmacological studies to express the decrease in serum levels following intravenous administration of a drug (Atkinson and Donev (1992), Chapter 18). A two-compartment model for predicting responses after a drug injection is

$$E[y(t)] = \alpha e^{-at} + \beta e^{-bt}, \quad w(t) = 1, \qquad t \in [0, c],$$

where $a > b$ and c are user-selected constants for the experiment. We therefore look for a maximum of the function $\psi(s,t) = [e^{-at-bs} - e^{-as-bt}]^2$. It is easily seen that the maximum will be reached on the boundary. Now, the function $\varphi(t,0)$ (defined in the proof of Proposition 3) reaches its absolute maximum at $t_0 = \frac{\log(\frac{a}{b})}{a-b}$, while $\varphi(t,c)$ reaches its absolute maximum at $t = 0$. Thus, the MIC is always satisfied and the maximal invariant set is $\{0, t_0\}$ if $t_0 \le c$ and is equal to $\{0, c\}$ if $t_0 \ge c$. Now we check if the condition (3.3) is true for these two cases.

If $t_0 \le c$ then $M = [(\frac{a}{b})^{-a/(a-b)} - (\frac{a}{b})^{-b/(a-b)}]^2$. The maximum of $\psi(t,0) + \psi(t,t_0)$ is M, and is attained at $t = 0$ and $t = t_0$. Therefore the condition (3.3) is verified and the equally weighted design at these points is D-optimal. On the other hand, if $t_0 \ge c$, we have $M = (e^{-bc} - e^{-ac})^2$ and the maximum of $\psi(t,0) + \psi(t,c)$ is M, attained at $t = 0$ and $t = c$. Therefore the condition (3.3) is also verified and the equally weighted design at these points is D-optimal. Other compartmental models can be analyzed in a similar manner.

4.2 *Segmented models*

These models are frequently used to study abrupt response behavioral changes in many biological studies, see Berman *et al.* (1996) for example. The simplest model assumes continuity and homoscedasticity and is given by

$$E[y(x)] = \begin{cases} \gamma + \delta x & \text{if} \quad x \in [-1, \alpha] \\ \tau + \beta x & \text{if} \quad x \in [\alpha, 1] \end{cases},$$

where α is assumed to be known. Following Park (1978), we reparametrize the mean response as

$$E[y(x)] = \gamma + \delta x + \beta T(x-\alpha), \qquad \text{where} \quad T(x) = \begin{cases} x & \text{if} \quad x \geq 0 \\ 0 & \text{if} \quad x \leq 0. \end{cases}$$

The maximum of the function $\psi(x,y,z)$ is reached only at $(-1,\alpha,1)$, and so $z_1 = -1$, $z_2 = \alpha$ and $z_3 = 1$ and the MIC is verified. Furthermore, the function $\psi(x,-1,\alpha)+\psi(x,-1,1)+\psi(x,\alpha,1)$ reaches its maximum exactly at the points $x = -1$, α and 1 and thus condition (3.3) holds. Consequently, the equally weighted design at ± 1 and α is D-optimal, as asserted in Park (1978).

4.3 *Truncated two-term polynomial model*

This example concerns truncated two-term polynomial models, where our two conditions can be easily checked. The model is

$$E[y(x)] = \alpha_1 x^k + \alpha_2 x^{k+r}, \qquad w(x) = 1, \qquad x \in [a,b], \qquad r \geq 1, \ k > 0$$

Proposition 3 says that MIC only can be true for two points. After differentiation it can be seen that one of the points must be a or b. Differentiating the functions $\varphi(a,x)$ and $\varphi(b,x)$ and solving the resulting equations to find the maximum, the possible points for the maximal invariant set are:

i) If r is even: a, b, $\pm a\sqrt[r]{\frac{k}{k+r}}$, $\pm b\sqrt[r]{\frac{k}{k+r}}$.

ii) If r is odd: a, b, $a\sqrt[r]{\frac{k}{k+r}}$, $b\sqrt[r]{\frac{k}{k+r}}$.

Two particularly interesting cases are $a = 0$ and $a = -b$. In the first case, the MIC is satisfied and the maximal invariant set is $\{b\sqrt[r]{\frac{k}{k+r}}, b\}$. In the latter case, the MIC is not verified if r is even but if r is odd the MIC is verified and the maximal invariant set is $\{-b, b\}$. For these two cases, the condition (3.3) is also true whenever the MIC holds.

4.4 *An example where $r > p$*

This example presents a case when $r > p$ and shows that r can attain the bound $p(p+1)/2$ given in Proposition 2. Suppose we have a simple linear model on the interval $[-1,1]$ and the efficiency function is

$$w(x) = \begin{cases} 1 & \text{if} \quad |x| \geq 1/2 \\ 6x+4 & \text{if} \quad -1/2 \leq x \leq 0 \\ -6x+4 & \text{if} \quad 0 \leq x \leq 1/2. \end{cases}$$

It is readily shown that the function $\psi(x,y) = w(x)w(y)[y-x]^2$ reaches its maximum at $(-1,0)$, $(-1,1)$ and $(0,1)$. Thus $z_1 = -1$, $z_2 = 0$, $z_3 = 1$ and $r = 3 = 2(2+1)/2 > 2 = p$. Thus, the MIC is verified and $M = 4$. Furthermore, the condition (3.3) is verified since $\sum_{i_2<\cdots<i_p} \psi(x, z_{i_2}, \ldots, z_{i_p}) = w(x)(6x^2+2)$ and this function attains its maximum at $x = -1$, 0 and 1. It follows that the design equally supported at -1, 0 and 1 is D-optimal.

4.5 *A maximal invariant set with interior points*

In all the previous examples, at least one point in the maximal invariant set is on the boundary of X. Here is an example where all of the points in the maximal invariant set are in the interior of X. Consider the model

$$E[y(x)] = \alpha_1 x + \alpha_2 \cos x, \qquad w(x) = 1, \qquad x \in [-\pi, 7\pi/2].$$

A similar calculation as before shows the MIC is true for the maximal invariant set is $\{6.38647, 9.58116\}$ and condition (3.3) holds with $M = 250.862$. Thus, the design equally supported on the set $\{6.38647, 9.58116\}$ is D-optimal.

5. Discussion

The MIC and the condition (3.3) are sufficient for an equally weighted design to be D-optimal. However, they are not necessary. To show this, consider again the simple linear model on the interval $[-1, 1]$ but this time the efficiency function is

$$w(x) = \begin{cases} 1 & \text{if } |x| \geq 2/3 \\ 2 & \text{if } |x| \leq 1/2 \\ 6x+5 & \text{if } -2/3 \leq x \leq -1/2 \\ -6x+5 & \text{if } 1/2 \leq x \leq 2/3. \end{cases}$$

For this problem, the function $\psi(x, y) = w(x)w(y)[y-x]^2$ reaches the maximum at $(-1/2, 1)$, $(1, -1/2)$, $(1/2, -1)$ and $(-1, 1/2)$, but not at $(-1/2, -1)$, for example. So, the MIC is not satisfied, and yet the design equally supported at ± 1 and $\pm 1/2$ is D-optimal (Fedorov (1972), p. 88).

Finally, we show it is possible that the MIC is satisfied but condition (3.3) is not valid. Here is a counter-example. The model is

$$E[y(x)] = \alpha_1 + \alpha_2 x + \alpha_3 x^4, \qquad w(x) = 1, \qquad x \in [-1, 1].$$

A direct calculation shows the function

$$\psi(x_1, x_2, x_3) = \begin{vmatrix} 1 & x_1 & x_1^4 \\ 1 & x_2 & x_2^4 \\ 1 & x_3 & x_3^4 \end{vmatrix}$$

reaches its maximum at $(-1, 0, 1)$ and at all other points with coordinates -1, 0 and 1. So, the MIC holds and the maximal invariant set is $\{-1, 0, 1\}$. In spite of this, no D-optimal design can be supported at three points (Landaw (1980), p. 225) and consequently, condition (3.3) cannot hold.

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