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THE OPTIMAL DESIGN OF AN EXPERIMENT WITH BLOCKS OF SIZE TWO FOR QUADRATIC REGRESSION ON ONE VARIABLE

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The Optimal Design of an Experiment with Blocks of Size Two for Quadratic Regression on One Variable

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Abstract

Exact $\mathcal{D}$-optimal designs are derived for an optometry experiment for the estimation of a quadratic polynomial in one explanatory variable. Two observations are made for each subject participating in the experiment, such that each subject serves as a block of two possibly correlated observations. The exact $\mathcal{D}$-optimal designs are compared to the best possible three-level designs and to the continuous $\mathcal{D}$-optimal designs.

Keywords: correlated observations, $\mathcal{D}$-optimality, optometry experiment, polynomial regression, random block effects

1 Introduction

The purpose of this paper is twofold. Firstly, it provides the reader with a series of exact $\mathcal{D}$-optimal designs for an optometry experiment with blocks of size two for the estimation of a quadratic model in one explanatory variable. It turns out that the designs presented here are substantially more efficient than the three level designs proposed by Chasalow (1992). Secondly, the paper provides the reader with a couple of interesting insights in the optimal design of experiments with correlated observations. It does not only demonstrate how the optimal designs depend on the extent to which the observations are correlated, but it also illustrates how the exact $\mathcal{D}$-optimal designs evolve towards the continuous $\mathcal{D}$-optimal designs derived by Cheng (1995) and Atkins and Cheng (1999) when the number of subjects available becomes large. In the next section, we give a concise description of the optometry experiment. The statistical model is introduced and the design criterion is derived in Section 3. The continuous $\mathcal{D}$-optimal designs are described in Section 4. In Section 5.1, we examine the $\mathcal{D}$-optimal three level designs for the optometry experiment obtained by Chasalow (1992). Finally, we derive exact $\mathcal{D}$-optimal designs for several numbers of subjects in Section 5.2.

2 Optometry experiment

Chasalow (1992) describes an optometry experiment to investigate the health impact of wearing contact lenses. One consequence of wearing contact lenses is that the corneas, which are the clear structures that cover the front parts of the eyes including the irises and the pupils (see Figure 1), are exposed to a decreased level of O_2. The decrease in O_2 leads to the production of a weak acid and an increased flow of water into the cornea. The cornea has active mechanisms for regulating the in- and outflow of water in order to counteract the effect of the decreased O_2 level and to avoid damage from excess swelling or dessication. The eye's ability to regulate the water content of the cornea is usually referred to as corneal hydration control and naturally tends to decrease with age. However, it turns out that people who have worn contact lenses for some time tend to have corneas that look like much older people, at least with respect to corneal hydration control. In the optometry experiment, the effect of wearing contact lenses was imitated by exposing the human subject's eyes to a CO_2 treatment. Once it has passed the tear film, CO_2 mixes with the aqueous component of the tears to form a weak acid and activates the water regulating mechanism of the cornea. The CO_2 treatments were applied through a goggle covering the subject's eyes.

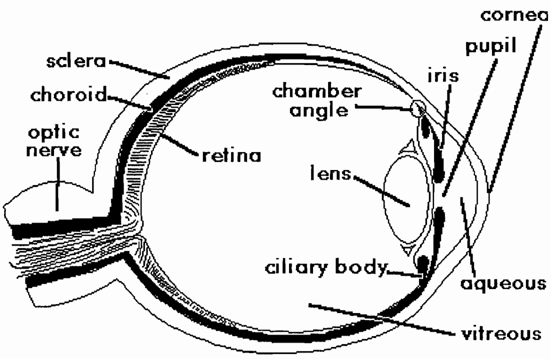

Figure 1: Anatomy of the eye.

The purpose of the experiment is to estimate a quadratic model in the CO_2 level that explains the variations in corneal hydration control. Every human subject in the study receives two treatments, one for each eye, yielding two observations per subject. The two treatments are allowed to be different. If we denote the number of subjects involved in the study by b, then the total number of observations in the study is equal to $n = 2b$. Of course, the two observations made for one subject are likely to be correlated, such that each subject serves as a block of two correlated observations. Typically, the number of subjects available lies between 30 and 60.

3 Model

Let us now denote by y a measure of the corneal hydration control and by x the level of the CO_2 treatment applied. The model of interest can then be written as

$$y = \beta_0 + \beta_1 x + \beta_2 x^2, \tag{1}$$

where β_0, β_1 and β_2 represent the intercept, the linear effect and the quadratic effect respectively. The statistical model corresponding to the experiment takes into account the random variation in each observation and the fact that each subject in the study is different. Therefore, the statistical model contains a random block effect for each subject in the study and an error term reflecting the random variation in each observation. The response of the jth observation for the ith subject can then be written as

$$y_{ij} = \beta_0 + \beta_1 x_{ij} + \beta_2 x_{ij}^2 + \gamma_i + \varepsilon_{ij}, \tag{2}$$

where x_{ij} is the jth CO_2 level applied to the ith subject, γ_i is the random effect corresponding to the ith subject and ε_{ij} is the random error. Since two measurements are made for each subject, the block size of the experiment is equal to two and the index j can only take the values 1 or 2. In matrix notation, the model becomes

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\boldsymbol{\gamma} + \boldsymbol{\varepsilon}, \tag{3}$$

where $\mathbf{y}$ is a vector of n observations on the corneal hydration control, the vector $\boldsymbol{\beta}$ contains the three unknown fixed parameters, the vector $\boldsymbol{\gamma} = [\ \gamma_1\ \gamma_2\ \ldots\ \gamma_b\ ]'$ contains the b random block effects and $\boldsymbol{\varepsilon}$ is an n-dimensional random error vector. The matrices $\mathbf{X}$ and $\mathbf{Z}$ are known and have dimension $n \times 3$ and $n \times b$ respectively. The n rows of $\mathbf{X}$ contain a one corresponding to the intercept, the CO_2 level for each observation and its square. The matrix $\mathbf{Z}$ assigns the treatments to the subjects. When the observations are grouped per subject, $\mathbf{Z}$ is of the form

$$\mathbf{Z} = \text{diag}[\mathbf{1}_2, \ldots, \mathbf{1}_2], \tag{4}$$

where $\mathbf{1}_2$ is a 2-dimensional vector of ones. It is assumed that

$$\text{E}(\boldsymbol{\varepsilon}) = \mathbf{0}_n \text{ and } \text{Cov}(\boldsymbol{\varepsilon}) = \sigma_\varepsilon^2 \mathbf{I}_n \tag{5}$$

$$\text{E}(\boldsymbol{\gamma}) = \mathbf{0}_b \text{ and } \text{Cov}(\boldsymbol{\gamma}) = \sigma_\gamma^2 \mathbf{I}_b \tag{6}$$

$$\text{Cov}(\boldsymbol{\gamma}, \boldsymbol{\varepsilon}) = \mathbf{0}_{b\times n}. \tag{7}$$

Under these assumptions, the variance-covariance matrix of the observations $\text{Cov}(\mathbf{y})$ can be written as

$$\mathbf{V} = \text{diag}[\tilde{\mathbf{V}}, \tilde{\mathbf{V}}, \ldots, \tilde{\mathbf{V}}], \tag{8}$$

where

$$\begin{aligned}\tilde{\mathbf{V}} &= \begin{bmatrix}\sigma_\varepsilon^2+\sigma_\gamma^2 & \sigma_\gamma^2\\ \sigma_\gamma^2 & \sigma_\varepsilon^2+\sigma_\gamma^2\end{bmatrix},\\ &= \sigma_\varepsilon^2\begin{bmatrix}1+\eta & \eta\\ \eta & 1+\eta\end{bmatrix},\end{aligned} \tag{9}$$

and $\eta = \sigma_\gamma^2/\sigma_\varepsilon^2$ is a measure for the extent to which observations within the same group are correlated. The larger η, the more the observations within one group are correlated. In the optometry experiment, it is expected that σ_γ^2 will be substantially larger than σ_ε^2, or, equivalently, that η will be substantially larger than one.

When the random error terms as well as the block effects are normally distributed, the maximum likelihood estimate of the unknown model parameter $\boldsymbol{\beta}$ in (3) is the generalized least squares (GLS) estimator

$$\hat{\boldsymbol{\beta}} = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^{-1}\mathbf{X}'\mathbf{V}^{-1}\mathbf{y}, \tag{10}$$

and the variance-covariance matrix of the estimators is given by

$$\mathrm{Var}(\hat{\boldsymbol{\beta}}) = (\mathbf{X}'\mathbf{V}^{-1}\mathbf{X})^{-1}. \tag{11}$$

The information matrix is given by the inverse of the variance-covariance matrix and is denoted by

$$\mathbf{M} = \mathbf{X}'\mathbf{V}^{-1}\mathbf{X}. \tag{12}$$

Using Theorem 18.2.8 of Harville (1997), we have that

$$\tilde{\mathbf{V}}^{-1} = \frac{1}{\sigma_\varepsilon^2}(\mathbf{I}_2 - c\mathbf{1}_2\mathbf{1}_2'), \tag{13}$$

where $c = \eta/(1+2\eta)$, and since $\mathbf{V}$ is block diagonal,

$$\begin{aligned}\mathbf{M} &= \sum_{i=1}^{b}\mathbf{X}_i'\tilde{\mathbf{V}}^{-1}\mathbf{X}_i\\ &= \frac{1}{\sigma_\varepsilon^2}\sum_{i=1}^{b}\mathbf{X}_i'(\mathbf{I}_2 - c\mathbf{1}_2\mathbf{1}_2')\mathbf{X}_i,\\ &= \frac{1}{\sigma_\varepsilon^2}\Big\{\sum_{i=1}^{b}(\mathbf{X}_i'\mathbf{X}_i - c\mathbf{X}_i'\mathbf{1}_2\mathbf{1}_2'\mathbf{X}_i)\Big\},\\ &= \frac{1}{\sigma_\varepsilon^2}\Big\{\mathbf{X}'\mathbf{X} - \sum_{i=1}^{b}c(\mathbf{X}_i'\mathbf{1}_2)(\mathbf{X}_i'\mathbf{1}_2)'\Big\},\end{aligned} \tag{14}$$

where $\mathbf{X}_i$ is the part of $\mathbf{X}$ corresponding to the ith subject.

The problem of designing the optometry experiment consists of choosing the CO_2 levels to be applied to the b subjects. In other words, the matrices $\mathbf{X}$ and $\mathbf{Z}$ have to be determined. In this paper, the $\mathcal{D}$-optimality criterion is used to compare alternative design options. The $\mathcal{D}$-optimal design maximizes the determinant of the information matrix (12) or (14). The problem of finding $\mathcal{D}$-optimal designs for the optometry experiment has already received attention by Chasalow (1992), Cheng (1995) and Atkins and Cheng (1999). Chasalow (1992) used complete enumeration to find the best possible exact designs with the levels -1, 0 and +1 for several numbers of subjects b. Cheng (1995) and Atkins and Cheng (1999) use an approximate theory to derive optimal continuous designs for the optometry experiment. We examine these results in some more detail in Section 4 and 5.1. In Section 5.2, we derive exact $\mathcal{D}$-optimal designs with b blocks of two observations for the estimation of the quadratic model (3). The resulting designs are much more efficient than the three level designs derived by Chasalow (1992). In the sequel of the paper, we denote the two treatments given to the ith subject by $(x_{i1}; x_{i2})$. The CO_2 level x is represented in coded form: its minimal and maximal value will be denoted by -1 and 1 respectively, hence $x_{ij} \in [-1, 1]$ $(i = 1, 2, \ldots, b; j = 1, 2)$.

4 Continuous $\mathcal{D}$-optimal designs

Cheng (1995) and Atkins and Cheng (1999) derive continuous $\mathcal{D}$-optimal designs for the optometry experiment. They show that the continuous $\mathcal{D}$-optimal design is supported on the blocks[1] $(1; -\alpha_\eta)$, $(-1; \alpha_\eta)$ and $(-1; 1)$, where $\alpha_\eta \geq 0$, with weights w_η, w_η and $1 - 2w_\eta$ respectively. Both α_η and w_η are increasing functions of η. Cheng (1995) shows that $\alpha_\eta \to 0$ and $w_\eta \to 1/3$ when η approaches zero. As an illustration, optimal values of α_η and w_η for several values of η are given in Table 1.

The continuous optimal designs for the optometry experiment possess four different factor levels: -1, $-\alpha_\eta$, α_η and 1. This is different from the continuous $\mathcal{D}$-optimal design for a model without block effects, which is supported on the levels -1, 0 and 1. It also turns out that the three blocks of the experiment do not receive equal weights when η is strictly positive. The blocks $(1; -\alpha_\eta)$ and $(-1; \alpha_\eta)$ both receive more weight than the block $(-1; 1)$. This is increasingly so when η increases. Finally, note that the pace with which α_η and w_η increase becomes very small for large values of η.

For the computation of continuous designs, it is assumed that an infinitely large number of blocks is available. In practice, however, this is not the case. In the next section, we compute exact $\mathcal{D}$-optimal designs for the optometry experiment and compare them to the designs obtained by rounding the $\mathcal{D}$-optimal continuous

[1] While a continuous design for an unblocked experiment is represented by a measure on the set of design points, a continuous design for a blocked experiment is represented by a measure on the set of blocks in the experiment.

Table 1: Values of α_η and w_η in the continuous $\mathcal{D}$-optimal design for the optometry experiment.

η	α_η	w_η	$1-2w_\eta$
0	0.000	0.333	0.333
0.1	0.029	0.334	0.331
0.25	0.059	0.338	0.324
0.5	0.093	0.345	0.311
0.75	0.115	0.351	0.299
1	0.131	0.356	0.288
2	0.167	0.370	0.260
5	0.202	0.386	0.228
10	0.218	0.394	0.212
100	0.234	0.403	0.193
∞	0.236	0.405	0.191

designs.

5 Exact $\mathcal{D}$-optimal designs

Chasalow (1992) computes the best possible exact designs with three factor levels, namely -1, 0 and 1, for the optometry experiment. His results are described in the first part of this section. In the second part, we show that the three-level designs can be improved to a large extent by using other factor levels as well.

5.1 Three-level designs

Chasalow (1992) uses complete enumeration to find the $\mathcal{D}$-optimal three-level designs for the optometry experiment for several values of b. It turns out that the optimal three-level designs are supported on three different blocks: $(1;0)$, $(-1;0)$ and $(-1;1)$. If b is a multiple of three, then each of the blocks is used $b/3$ times in the $\mathcal{D}$-optimal design. In that case, the $\mathcal{D}$-optimal design is a balanced incomplete block design. If b is not a multiple of three, the three types of blocks are used with frequencies as equal as possible. Cheng (1995) shows that the designs derived by Chasalow are $\mathcal{D}$-optimal among all minimum support designs —that is the set of designs with p distinct design points— for any strictly positive η.

5.2 $\mathcal{D}$-optimal designs

The three-level designs described in Section 5.1 are not optimal when the number of support points is allowed to be more than the number of fixed model parameters p. In this section, we show that the $\mathcal{D}$-optimal designs for the optometry experiment possess four factor levels. The $\mathcal{D}$-optimal designs are computed by combining the blocking algorithm of Goos and Vandebroek (2001) and the adjustment algorithm of Donev and Atkinson (1988). Analytical results for small numbers of b are used to evaluate this approach.

5.2.1 Computing the $\mathcal{D}$-optimal designs

We have computed the $\mathcal{D}$-optimal designs for the optometry experiment by combining the point exchange algorithm of Goos and Vandebroek (2001) and the adjustment algorithm of Donev and Atkinson (1988). The algorithm of Goos and Vandebroek computes $\mathcal{D}$-optimal response surface designs in the presence of random block effects for a given number of blocks b, block size k and degree of correlation η. As in many other design construction algorithms, the design points are chosen from a set of candidate points. The algorithm produces the $\mathcal{D}$-optimal three-level designs described in Section 5.1 when the default set of the candidate points -1, 0 and +1 is used. However, it produces substantially better designs when a set of 21 equally spaced points between -1 and 1 is used. The adjustment algorithm of Donev and Atkinson is a method to improve the design obtained from a search over a grid. It calculates the effect of moving each design point a small amount, called a step, along each factor axis. The change that generates the greatest improvement is carried out and the process is repeated until no further progress can be made. If no improvement can be found, the step length is halved and the process is repeated. The algorithm stops when the step length becomes smaller than a prespecified minimum step length. The maximum number of changes evaluated is $2mn$, where m is the number of experimental factors. For the optometry experiment, $m = 1$ and the maximum number of changes is $2n$. When one or more design points lie on the boundary of the experimental region $[-1, 1]$, the number of changes evaluated is less than $2n$ because points outside the experimental region are omitted. It turns out that the initial step size and the speed of the step-length reduction do not influence the efficiency of the resulting designs. A formal description of the adjustment algorithm is given in the Appendix. The algorithm was implemented in FORTRAN 77 and is available from the authors. In the sequel of this section, we will describe the computational results for several values of b. For small values of b, analytical results are used to evaluate the performance of the algorithmic approach.

5.2.2 Designs with 2 blocks

First, consider the problem of designing an optometry experiment with two blocks of two observations. Hence $b = 2$ and $n = 4$. When $\eta = 0$, the design problem reduces to the computation of a 4-point $\mathcal{D}$-optimal completely randomized design, which has observations in the points -1, 0 and 1, one of which is duplicated. Typically, the symmetric design with the duplicated center point will be preferred because the linear effect can then be estimated independently of the intercept and the quadratic

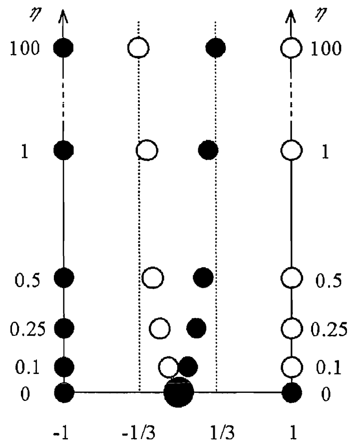

Figure 2: $\mathcal{D}$-optimal design points for the optometry experiment when $b = 2$. A $\bullet$ indicates a design point from block 1, a $\circ$ indicates a design point from block 2.

effect. When $\eta > 0$, the $\mathcal{D}$-optimal designs generated by the algorithmic approach have four different factor levels: -1, $-a_\eta$, a_η and 1, where $a_\eta > 0$. The first block of the optimal design contains the points -1 and a_η. The second block contains the points $-a_\eta$ and 1. It turns out that a smaller η results in a smaller a_η. When $\eta \to 0$, $a_\eta \to 0$. A similar result was found for continuous designs. We have displayed the optimal design points for several values of η in Figure 2. The figure clearly shows that a_η increases as η increases. Now, we will show how the exact $\mathcal{D}$-optimal values for a_η can be computed analytically. It will also be shown that a_η approaches 1/3 when $\eta \to \infty$.

For notational simplicity, assume without loss of generality that $\sigma_\varepsilon^2 = 1$. Substituting $b = 2$, in (14), we then have

$$\mathbf{X}'\mathbf{V}^{-1}\mathbf{X} = \mathbf{X}'\mathbf{X} - c\sum_{i=1}^{2}(\mathbf{X}_i'\mathbf{1}_2)(\mathbf{X}_i'\mathbf{1}_2)'. \tag{15}$$

For the design problem at hand, the optimal design is of the form

$$\mathbf{X} = \begin{bmatrix}\mathbf{X}_1\\ \mathbf{X}_2\end{bmatrix} = \begin{bmatrix}1 & -1 & 1\\ 1 & a_\eta & a_\eta^2\\ 1 & -a_\eta & a_\eta^2\\ 1 & 1 & 1\end{bmatrix},$$

with

$$\mathbf{X}_1 = \begin{bmatrix}1 & -1 & 1\\ 1 & a_\eta & a_\eta^2\end{bmatrix} \text{ and } \mathbf{X}_2 = \begin{bmatrix}1 & -a_\eta & a_\eta^2\\ 1 & 1 & 1\end{bmatrix}.$$

Table 2: $\mathcal{D}$-optimal values for a_η when 2 blocks of size 2 are used for quadratic regression on one variable.

η	c	κ	λ	a_η
0.1	0.0833	7.3889	-26.3241	0.085685
0.25	0.1667	5.5556	-42.5926	0.161359
0.5	0.2500	3.5000	-49.2500	0.220333
1	0.3333	1.2222	-46.7407	0.266218
2	0.4000	-0.7600	-38.4320	0.296215
5	0.4545	-2.4876	-27.6409	0.317454
10	0.4762	-3.1996	-22.3928	0.325202
100	0.4975	-3.9155	-16.6980	0.332502
∞	0.5000	-4.0000	-16.0000	0.333333

Substituting these results in (15), yields the following information matrix:

$$\mathbf{X}'\mathbf{V}^{-1}\mathbf{X} = 2\begin{bmatrix} 2-4c & 0 & (1-2c)(1+a_\eta^2) \\ 0 & 1+a_\eta^2 - c(a_\eta - 1)^2 & 0 \\ (1-2c)(1+a_\eta^2) & 0 & 1+a_\eta^4 - c(1+a_\eta^2)^2 \end{bmatrix}.$$

The determinant of this matrix reaches a maximum when its first derivative with respect to a_η is zero and its second derivative with respect to a_η is strictly negative. These conditions are satisfied for

$$a_\eta = \frac{1}{9(1-c)}\left(-5c + \frac{\kappa\sqrt[3]{2}}{\sqrt[3]{\lambda + \sqrt{4\kappa^3 + \lambda^2}}} - \frac{\sqrt[3]{\lambda + \sqrt{4\kappa^3 + \lambda^2}}}{\sqrt[3]{2}}\right), \tag{16}$$

with

$$\kappa = 9 - 18c - 16c^2 \text{ and } \lambda = -243(1-c)^2 c + 135(1-c)(c-1)c + 250c^3.$$

Substituting different values for c in (16) yields the corresponding optimal value for a_η. For example, when $\eta = 1$, $c = 1/3$, $\kappa = 11/9$ and $\lambda = -47 + 7/27$. As a result, the optimal value for a_η is 0.266218. We have performed similar computations for other values of η. The results are given in Table 2. When $\eta \to \infty$, $c \to 1/2$, $\kappa \to -4$ and $\lambda \to -16$. As a consequence, $a_\eta \to 1/3$ when $\eta \to \infty$.

5.2.3 Designs with 3 blocks

Now, consider the problem of designing an optometry experiment with three blocks. When $\eta = 0$, the $\mathcal{D}$-optimal design has two observations in the points -1, 0 and 1. When $\eta > 0$, the algorithmic approach again produces designs with four different factor levels: -1, $-b_\eta$, b_η and 1, where $b_\eta > 0$. The first block of the optimal design contains the points -1 and 1. The second block contains the points -1 and b_η and

Table 3: $\mathcal{D}$-optimal values for b_η when 3 blocks of size 2 are used for quadratic regression on one variable.

η	c	θ	τ	b_η
0.1	0.0833	23.8889	-46.9491	0.028434
0.25	0.1667	20.5556	-80.0926	0.057676
0.5	0.2500	17.000	-99.8750	0.086936
1	0.3333	13.2222	-106.7407	0.115506
2	0.4000	10.0400	-103.2320	0.137503
5	0.4545	7.3306	-94.5830	0.154793
10	0.4762	6.2290	-89.7398	0.161464
100	0.4975	5.1293	-84.1963	0.167924
∞	0.5000	5.0000	-83.5000	0.168663

the third block contains the points $-b_\eta$ and 1. It turns out that b_η increases with η. This result does not come as a surprise in view of the results of Cheng (1995), who proves that the $\mathcal{D}$-optimal continuous design for the design problem at hand is supported on three blocks with a similar structure (see Section 4). Analytical computations analogous to those for $b = 2$ show that the $\mathcal{D}$-optimal value for b_η is given by

$$b_\eta = \frac{1}{9(1-c)}\left(-5c + \frac{\theta\sqrt[3]{2}}{\sqrt[3]{\tau + \sqrt{4\theta^3 + \tau^2}}} - \frac{\sqrt[3]{\tau + \sqrt{4\theta^3 + \tau^2}}}{\sqrt[3]{2}}\right), \tag{17}$$

with

$$\theta = 27 - 36c - 16c^2 \text{ and } \tau = -243(1-c)^2 c + 135(1-c)(c-3)c + 250c^3.$$

In Table 3, $\mathcal{D}$-optimal values for b_η are given for several values of η. The values found are different from those found by Cheng (1995) for the $\mathcal{D}$-optimal continuous design. This is because the $\mathcal{D}$-optimal continuous design does not have an equal weight on the three blocks whereas in the discrete case, the weight of each block is equal to one.

The algorithmic approach produces values for a_η and b_η that closely approximate the ones analytically derived and displayed in Tables 2 and 3. This is illustrated in Table 4.

5.2.4 Designs with 4 or 5 blocks

The structure of the $\mathcal{D}$-optimal designs with two or three blocks of size 2 for quadratic regression on one variable appears to be constant for all values of η. As is demonstrated by the optimal designs for $b = 4$ displayed in Table 5, this is not always the case for larger values of b. In the table, the numbers r_i represent the number of times the ith type of block is used in the experiment. When $b = 4$

Table 4: Comparison of the $\mathcal{D}$-optimal values for a_η and b_η and the values computed by the adjustment algorithm (A.A.).

	a_η		b_η	
η	Exact	A.A.	Exact	A.A.
0.1	0.085685	0.085000	0.028434	0.027500
0.25	0.161359	0.160000	0.057676	0.057500
0.5	0.220333	0.220000	0.086936	0.087500
1	0.266218	0.267500	0.115506	0.115000
2	0.296215	0.297500	0.137503	0.137500
5	0.317454	0.317500	0.154793	0.155000
10	0.325202	0.325000	0.161464	0.162500
100	0.332502	0.332500	0.167924	0.167500

and η is small, two equivalent $\mathcal{D}$-optimal designs are supported on three different blocks. One design is supported on the blocks $(-1; c_\eta)$, $(-d_\eta; 1)$ and $(-1; 1)$, with $0 < c_\eta < d_\eta$. The block $(-1; c_\eta)$ appears twice in the optimal design, while the other two blocks appear only once. The mirror image of this design, obtained by multiplying its factor levels by -1, is equivalent. It turns out that both c_η and d_η are increasing functions of η. When η is large, the $\mathcal{D}$-optimal designs with four blocks are supported on two different blocks $(-1; f_\eta)$ and $(-f_\eta; 1)$, with $0 < f_\eta$ and f_η an increasing function of η. Both blocks are replicated twice. When $b = 5$, the $\mathcal{D}$-optimal designs have two blocks of type $(-1; g_\eta)$, two blocks of type $(-g_\eta; 1)$ and one block of type $(-1; 1)$, where $g_\eta > 0$ and increases with η. Some $\mathcal{D}$-optimal values of g_η are given in Table 5.

5.2.5 Large numbers of blocks

As for $b = 4$, the structure of the exact $\mathcal{D}$-optimal designs with large numbers of blocks is not constant for all values of η. In addition, there is a growing resemblance between the exact $\mathcal{D}$-optimal designs and the continuous $\mathcal{D}$-optimal designs when b is further increased. The exact $\mathcal{D}$-optimal designs are then supported on blocks of type $(-1, s_\eta)$ and $(-t_\eta, 1)$, with $0 < s_\eta$ and $0 < t_\eta$, and on the block $(-1, 1)$. The mirror images of these designs are $\mathcal{D}$-optimal as well. Not surprizingly, s_η and t_η are increasing functions of η. In the optimal designs, the first two blocks are used with frequencies as equal as possible. Therefore, the absolute difference between r_1 and r_2 is at most one. In all cases where r_1 is equal to r_2, s_η and t_η are equal as well. In cases where r_1 and r_2 are different, $s_\eta < t_\eta$ when $r_1 = r_2 + 1$ and $s_\eta > t_\eta$ when $r_1 = r_2 - 1$. Some examples of $\mathcal{D}$-optimal values for r_1, r_2, r_3, s_η and t_η are given in the left hand panel of Table 6. For example, a $\mathcal{D}$-optimal design for $b = 49$ and $\eta = 1$ contains 18 blocks of type (-1;0.129), 17 blocks of type (-0.135;1) and 14 blocks of type (-1;1).

Table 5: $\mathcal{D}$-optimal designs with four or five blocks.

b	η	r_1	Block 1	r_2	Block 2	r_3	Block 3
4	0.1	2	(-1;0.025)	1	(-0.050;1)	1	(-1;1)
		1	(-1;0.050)	2	(-0.025;1)	1	(-1;1)
	0.5	2	(-1;0.080)	1	(-0.145;1)	1	(-1;1)
		1	(-1;0.145)	2	(-0.080;1)	1	(-1;1)
	1	2	(-1;0.106)	1	(-0.185;1)	1	(-1;1)
		1	(-1;0.185)	2	(-0.106;1)	1	(-1;1)
	5	2	(-1;0.318)	2	(-0.318;1)		
	10	2	(-1;0.325)	2	(-0.325;1)		
5	0.1	2	(-1;0.043)	2	(-0.043;1)	1	(-1;1)
	0.5	2	(-1;0.129)	2	(-0.129;1)	1	(-1;1)
	1	2	(-1;0.168)	2	(-0.168;1)	1	(-1;1)
	5	2	(-1;0.215)	2	(-0.215;1)	1	(-1;1)
	10	2	(-1;0.223)	2	(-0.223;1)	1	(-1;1)

5.2.6 Efficiency comparisons

Comparing the exact $\mathcal{D}$-optimal designs with the three-level designs described in Section 5.1 in terms of $\mathcal{D}$-efficiency shows that the former are more efficient than the latter, especially for large degrees of correlation. For $b = 2$, the exact $\mathcal{D}$-optimal design is 0.26% more efficient than the best three-level design when $\eta = 0.1$, whereas it is 9.68% more efficient when $\eta = 10$. For $b = 5$, the $\mathcal{D}$-optimal design is 0.08% more efficient when $\eta = 0.1$ and 3.51% more efficient when $\eta = 10$. For large b, the efficiency comparisons are given in the middle panel of Table 6. For $\eta = 0.1$, the three-level designs are on average 0.04% less efficient than the $\mathcal{D}$-optimal ones. However, they are 2.25% less efficient when $\eta = 10$. This is not unexpected because the $\mathcal{D}$-optimal designs for small η strongly resemble the three-level designs, while both the design points and the numbers of replicates of the blocks are completely different for larger values of η. The relative performance of the designs is independent of the number of subjects available, provided it is large.

For large numbers of subjects, rounding the continuous $\mathcal{D}$-optimal design, that is setting $r_1 = r_2 = [bw_\eta]$ and $r_3 = b - r_1 - r_2$, turns out to be a good design option, although it does not yield the exact $\mathcal{D}$-optimal design. Firstly, the factor levels obtained by rounding the continuous design are slightly different from those of the exact $\mathcal{D}$-optimal design. Secondly, rounding the weights w_η and $1 - 2w_\eta$ of the continuous design does not always produce the optimal numbers of replicates r_i. Suppose, we would like to construct a design with 49 blocks from the $\mathcal{D}$-optimal continuous design for $\eta = 1$. As can be seen from Table 1, the weight w_η assigned to the blocks of type $(-1; 0.131)$ and $(-0.131; 1)$ is 0.356. In a design with 49 blocks, this type of block should thus be used $49 \times 0.356 = 17.444$ times. Rounding this value to the nearest integer gives us $r_1 = r_2 = 17$, and hence $r_3 = 15$. The resulting $\mathcal{D}$-criterion value is nearly identical to that of the $\mathcal{D}$-optimal design with $r_1 = 18$, $r_2 = 17$ and $r_3 = 14$ given in Table 6. As a result, rounding the continuous $\mathcal{D}$-optimal design produces a design that is only slightly less efficient than the $\mathcal{D}$-optimal design. This is also the case for other values of b and η, even though the factor levels α_η of the continuous designs are different from the levels of the exact $\mathcal{D}$-optimal designs. This is illustrated in the right panel of Table 6.

6 Discussion

A common feature of all $\mathcal{D}$-optimal designs for the problem under consideration is that they possess four different design points. As was illustrated in Figure 2, the design points move away from the center point when the degree of correlation η grows larger. In addition, the number of times r_3 the block $(-1; 1)$ appears in the optimal designs decreases with increasing η, while the opposite is true for the other blocks. A similar behaviour was encountered when examining the continuous $\mathcal{D}$-optimal designs.

It turns out that the exact $\mathcal{D}$-optimal designs are substantially more efficient than the best possible three-level designs, especially for the large degrees of correlation experienced in practice. It is thus worthwhile to consider other factor levels than -1, 0 and 1 when designing the optometry experiment. It also turns out that, although it does not produce the exact $\mathcal{D}$-optimal design, rounding the continuous $\mathcal{D}$-optimal designs is an excellent design option for this design problem, such that an algorithmic approach does not add much value. From a practical point of view, it is also important to stress that the efficiency of the designs obtained in this way does not heavily depend on η. This is because both the factor levels and the block weights of the continuous designs do not vary much when η is large as is mostly the case in practical applications.

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Appendix: The adjustment algorithm.

We denote by s the step length and by S the minimum step length. Let the starting design $D = \{1, 2, \ldots, n\}$ be composed of n design points with coordinates $\mathbf{c}_i = (c_{i1}, c_{i2}, \ldots, c_{im})$, $i = 1, 2, \ldots, n$, let J be the set of all integers up to m and let K

Table 6: Comparison of three design options for the optometry experiment. The number of replicates of block i is denoted by r_i. For all design options in the table, block 3 is given by (-1;1).

DESIGN PROBLEM		DESIGN OPTIONS														
		EXACT D-OPTIMAL DESIGNS					THREE-LEVEL DESIGNS					ROUNDED CONTINUOUS D-OPTIMAL DESIGNS				
b	η	r_1	r_2	r_3	Block 1	Block 2	$r_1 = r_2$	r_3	Block 1	Block 2	rel.eff.	$r_1 = r_2$	r_3	Block 1	Block 2	rel.eff.
36	0.1	12	12	12	(-1;0.028)	(-0.028;1)	12	12	(-1;0)	(0;1)	0.999587	12	12	(-1;0.029)	(-0.029;1)	0.999999
	0.5	13	12	11	(-1;0.091)	(-0.098;1)	12	12	(-1;0)	(0;1)	0.995755	12	12	(-1;0.093)	(-0.093;1)	0.999898
	1	13	13	10	(-1;0.135)	(-0.135;1)	12	12	(-1;0)	(0;1)	0.991312	13	10	(-1;0.131)	(-0.131;1)	0.999990
	5	14	14	8	(-1;0.205)	(-0.205;1)	12	12	(-1;0)	(0;1)	0.980342	14	8	(-1;0.202)	(-0.202;1)	0.999995
	10	14	14	8	(-1;0.212)	(-0.212;1)	12	12	(-1;0)	(0;1)	0.977565	14	8	(-1;0.218)	(-0.218;1)	0.999975
48	0.1	16	16	16	(-1;0.028)	(-0.028;1)	16	16	(-1;0)	(0;1)	0.999588	16	16	(-1;0.029)	(-0.029;1)	1.000000
	0.5	17	16	15	(-1;0.090)	(-0.095;1)	16	16	(-1;0)	(0;1)	0.995669	17	14	(-1;0.093)	(-0.093;1)	0.999887
	1	17	17	14	(-1;0.130)	(-0.130;1)	16	16	(-1;0)	(0;1)	0.991267	17	14	(-1;0.131)	(-0.131;1)	0.999999
	5	19	18	11	(-1;0.198)	(-0.205;1)	16	16	(-1;0)	(0;1)	0.980452	19	10	(-1;0.202)	(-0.202;1)	0.999927
	10	19	19	10	(-1;0.219)	(-0.219;1)	16	16	(-1;0)	(0;1)	0.977539	19	10	(-1;0.218)	(-0.218;1)	0.999999
49	0.1	17	16	16	(-1;0.028)	(-0.030;1)	16	17	(-1;0)	(0;1)	0.999572	16	17	(-1;0.029)	(-0.029;1)	0.999954
	0.5	17	17	15	(-1;0.094)	(-0.094;1)	16	17	(-1;0)	(0;1)	0.995479	17	15	(-1;0.093)	(-0.093;1)	0.999999
	1	18	17	14	(-1;0.129)	(-0.135;1)	16	17	(-1;0)	(0;1)	0.991245	17	15	(-1;0.131)	(-0.131;1)	0.999925
	5	19	19	11	(-1;0.204)	(-0.204;1)	16	17	(-1;0)	(0;1)	0.980207	19	11	(-1;0.202)	(-0.202;1)	0.999998
	10	19	19	11	(-1;0.211)	(-0.211;1)	16	17	(-1;0)	(0;1)	0.977459	19	11	(-1;0.218)	(-0.218;1)	0.999965
60	0.1	20	20	20	(-1;0.028)	(-0.028;1)	20	20	(-1;0)	(0;1)	0.999588	20	20	(-1;0.029)	(-0.029;1)	1.000000
	0.5	21	21	18	(-1;0.096)	(-0.096;1)	20	20	(-1;0)	(0;1)	0.995639	21	18	(-1;0.093)	(-0.093;1)	0.999995
	1	21	21	18	(-1;0.127)	(-0.127;1)	20	20	(-1;0)	(0;1)	0.991327	21	18	(-1;0.131)	(-0.131;1)	0.999990
	5	23	23	14	(-1;0.199)	(-0.199;1)	20	20	(-1;0)	(0;1)	0.980344	23	14	(-1;0.202)	(-0.202;1)	0.999995
	10	24	24	12	(-1;0.223)	(-0.223;1)	20	20	(-1;0)	(0;1)	0.977578	24	12	(-1;0.218)	(-0.218;1)	0.999979

be the set of the integers 1 and 2. The steps of the adjustment algorithm are as follows:

1. Specify s and S.
2. Compute the determinant $\mathcal{D}$ and the information matrix $\mathbf{M}$ of the starting design.
3. Evaluate design changes.
   (a) Set $\delta = 1$.
   (b) $\forall i \in D, \forall j \in J, \forall k \in K$:
      i. Compute the effect $\delta_{ijk} = \mathcal{D}'/\mathcal{D}$ of replacing the jth coordinate of the ith design point c_{ij} with $c_{ij} + s \times (-1)^k$.
      ii. If $\delta_{ijk} > \delta$, then $\delta = \delta_{ijk}$ and store $i^* = i$, $j^* = j$ and $k^* = k$.
4. If $\delta > 1$, then go to step 5, else go to step 6.
5. Carry out the best exchange.
   (a) Replace $c_{i^*j^*}$ with $c_{i^*j^*} + s \times (-1)^{k^*}$.
   (b) Update $\mathcal{D}$ and $\mathbf{M}$ and go to step 3.
6. Set $s = s/2$.
7. If $s \geq S$, go to step 3, else stop.

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