# E-optimal designs under an interference model Katarzyna Filipiak<sup>1</sup>, Rafał Różański<sup>2</sup>

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## **SUMMARY**

In this paper, experiments with the same number of treatments, blocks and plots are considered. It is assumed that the response to a treatment is affected by other treatments, and so the model of the experiment is an interference model with neighbor effects. The aim of this paper is to identify the structure of the left-neighbor matrix of E-optimal design and to give the method of construction of such design.

Key words: complete block design; interference model; information matrix; E-optimality

## 1. Introduction

In the theory of experimental designs, optimality of designs is often considered. It is known, for example, that balanced incomplete block designs (BIBD) are universally optimal under the model with block effects as the only nuisance parameters. However, in some experiments interplot interference may occur, and then the optimality of designs under an interference model is studied. Recently, some results on optimality of binary designs under an interference model with neighbor effects have been published. These results concern mainly binary designs, such as circular neighbor balanced designs and orthogonal arrays of type I. It was shown that circular neighbor balanced designs are universally optimal for estimating treatment effects under a fixed interference model (Druilhet, 1999), under a mixed interference model (Filipiak and Markiewicz, 2003), and under the fixed interference model with correlated observations (Filipiak and Markiewicz, 2005). Bailey and Druilhet (2004) showed optimality of these designs under a fixed interference model for estimating of the sum of treatment and neighbor effects. Universal optimality of orthogonal arrays

of type I under a general interference model with correlated observations is shown in Filipiak and Markiewicz (2004).

It is known, however, that circular neighbor balanced designs and orthogonal arrays cannot exist for each combination of design parameters. In such a situation, only the optimality with respect to the specified optimality criteria can be studied. The aim of this paper is to determine E-optimal design under an interference model, i.e. such design that the maximal variance among all best linear unbiased estimators of normalized linear contrasts is minimal under this design; cf. Constantine, 1981.

In this paper, E-optimality of binary block designs under an interference model with left-neighbor effects is studied. As an example we consider binary block designs with the same number of treatments t and plots k (t = k), i.e. complete block designs. Such designs are often used in practice. For example, in UPOV research (the International Union for the Protection of New Varieties of Plants research), complete block designs are used in experiments in which the number of treatments is less than 16. Moreover, we assume that in complete block designs the number of blocks, b, is the same as the number of treatments and plots (i.e. t = b = k), because for such design parameters circular neighbor balanced designs, which are universally optimal under the interference model, cannot exist. Such experiments can be applied in clinical trials.

This paper is organized as follows. We start by presenting an interference model with neighbor effects. In Section 3 we give the form and properties of the information matrix of the design, which will be used in determining E-optimal design. In Section 4 we give conditions for the structures of the left-neighbor matrices of E-optimal complete block designs for a class of designs with t = b = k. For  $3 \le t \le 10$  we present the method of construction of E-optimal designs and examples of such designs for specified t.

#### 2. Interference model

Let  $I_n$  denote an  $n \times n$  identity matrix,  $1_n$  denote an n-dimensional column vector of ones,  $0_n$  denote an n-dimensional column vector of zeros, and the symbol  $\otimes$  denote the Kronecker product.

Consider a set of block designs  $\mathcal{D}_{t,b,k}$ , with t treatments arranged on bk plots, which are grouped in b blocks. An interference model associated with the design  $d \in \mathcal{D}_{t,b,k}$  can be written as

$$\mathbf{y} = \mathbf{T}_{d}\tau + \mathbf{L}_{d}\lambda + \mathbf{B}\boldsymbol{\beta} + \boldsymbol{\varepsilon},\tag{1}$$

where  $\tau$ ,  $\lambda$  and  $\beta$  are the vectors of treatment effects, left-neighbor effects and block effects, respectively. Here  $\varepsilon$  is a vector of random errors,  $\varepsilon \sim N(0, \sigma^2 \mathbf{I}_{bk})$ , where  $\sigma^2$  is a positive unknown constant. The assumption that each block of the

design has the same number of plots implies  $\mathbf{B} = \mathbf{I}_h \otimes \mathbf{1}_k$ .

Let  $T_{du}$  be the design matrix of treatment effects in block u,  $1 \le u \le b$ . Further, define  $T_d = (T'_{d1} : ... : T'_{db})'$  as the design matrix of treatment effects. For each u we define  $L_{du} = H_k T_{du}$ , where  $H_k$  is an  $k \times k$  matrix of the form

$$\mathbf{H}_{k} = \begin{pmatrix} \mathbf{0}_{k-1}^{'} & 1 \\ \mathbf{I}_{k-1} & \mathbf{0}_{k-1} \end{pmatrix}. \tag{2}$$

Then,  $L_d = (I_b \otimes H_k)T_d$  is the design matrix of left-neighbor effects. Model (1) with  $H_k$  and  $L_d$  defined above, is called a circular interference model with left-neighbor effects.

The matrices  $T_d$  and  $L_d$  depend on the arrangement of treatments on plots, i.e. they change with the design, while the matrix **B** is the same for each design  $d \in \mathcal{D}_{t,b,k}$ . Thus, the matrices  $T_d$  and  $L_d$  are indexed by d.

We will consider designs in which each treatment has a left neighbor. This situation may occur if each block of a design has the form of a circle. If plots in blocks are arranged in linear forms, we can obtain the effect of circularity by adding border plots at the beginning of each block, where the treatment at the border plot is the same as the treatment at the opposite end of the block. For example, the design with border plots, with 4 treatments, arranged on 6 plots in 2 blocks, has the form:

$$\begin{pmatrix}
4 & 1 & 2 & 4 \\
2 & 3 & 3 & 2
\end{pmatrix}$$

Border plots are not used for measuring the response variables.

#### 3. Information matrix

Let  $C_d$  denote the information matrix of design d for estimating  $\tau$  in the linear model under normality. Following Markiewicz (1997), the information matrix  $C_d$  can be expressed as a function of the information matrix for the simultaneous estimation of  $\tau$  and  $\lambda$ , of the form

$$\mathbf{W}_d = (\mathbf{T}_d : \mathbf{L}_d)' \mathbf{Q}_B(\mathbf{T}_d : \mathbf{L}_d),$$

where  $\mathbf{Q}_B = \mathbf{I}_{bk} - \mathbf{B}(\mathbf{B}'\mathbf{B})^{-}\mathbf{B}$  is the orthogonal projector onto the orthocomplement of the column span of  $\mathbf{B}$ , where  $(\mathbf{B}'\mathbf{B})^{-}$  denotes a generalized inverse of  $\mathbf{B}'\mathbf{B}$ . For  $\mathbf{B} = \mathbf{I}_b \otimes \mathbf{I}_k$  we obtain  $\mathbf{Q}_B = \mathbf{I}_b \otimes \mathbf{E}_k$ , where  $\mathbf{E}_k = \mathbf{I}_k - k^{-1}\mathbf{1}_k\mathbf{I}_k$ .

The properties of the information matrix  $C_d$  as a function of  $W_d$ , are presented in Pukelsheim (1993) and Markiewicz (1997). In particular, the information matrix  $C_d$  can be expressed as the Schur complement of the matrix  $L'_d Q_B L_d$  in  $W_d$ , i.e.

$$\mathbf{C}_d = [\mathbf{W}_d / \mathbf{L}_d' \mathbf{Q}_B \mathbf{L}_d] = \mathbf{T}_d' \mathbf{Q}_B \mathbf{T}_d - \mathbf{T}_d' \mathbf{Q}_B \mathbf{L}_d (\mathbf{L}_d' \mathbf{Q}_B \mathbf{L}_d)^{\mathsf{T}} \mathbf{L}_d' \mathbf{Q}_B \mathbf{T}_d. \tag{3}$$

Observe that the matrix  $\mathbf{Q}_B$  has row and column sums zero. Since vectors  $\mathbf{T}_d \mathbf{I}_t$  and  $\mathbf{L}_d \mathbf{I}_t$  are in the column-space of  $\mathbf{B}$ , each block of the matrix  $\mathbf{W}_d$  has zero row and column sums. Moreover, observe that  $\mathbf{H}_k$  defined in (2) is a permutation matrix. It implies that  $\mathbf{H}_k \mathbf{E}_k \mathbf{H}_k' = \mathbf{H}_k' \mathbf{E}_k \mathbf{H}_k = \mathbf{E}_k$ . Hence, the block matrices of  $\mathbf{W}_d$  are of the form:

$$\begin{split} \mathbf{T}_{d}^{'}\mathbf{Q}_{B}\mathbf{T}_{d} &= \mathbf{T}_{d}^{'}\mathbf{T}_{d} - \frac{1}{k}\sum_{u=1}^{b}\mathbf{T}_{du}^{'}\mathbf{1}_{l}\mathbf{1}_{l}^{'}\mathbf{T}_{du}, \\ \mathbf{T}_{d}^{'}\mathbf{Q}_{B}\mathbf{L}_{d} &= \mathbf{T}_{d}^{'}\mathbf{L}_{d} - \frac{1}{k}\sum_{u=1}^{b}\mathbf{T}_{du}^{'}\mathbf{1}_{l}\mathbf{1}_{l}^{'}\mathbf{L}_{du} \quad \text{and} \quad \mathbf{L}_{l}^{'}\mathbf{Q}_{B}\mathbf{L}_{d} &= \mathbf{T}_{l}^{'}\mathbf{Q}_{B}\mathbf{T}_{d}. \end{split}$$

In this paper we consider complete binary designs with the same number of blocks as plots and treatments, i.e. binary designs with t = b = k. We will denote the set of such designs by  $\mathcal{D}_t$ . For each block of design  $d \in \mathcal{D}_t$  we have  $\mathbf{T}'_{du} \mathbf{1}_t = \mathbf{L}'_{du} \mathbf{1}_t = \mathbf{1}_t$ . Hence

$$\mathbf{T}_d'\mathbf{Q}_B\mathbf{T}_d = t\mathbf{I}_t - \mathbf{1}_t\mathbf{1}_t' = t\mathbf{E}_t$$
 and  $\mathbf{T}_d'\mathbf{Q}_B\mathbf{L}_d = \mathbf{T}_d'\mathbf{L}_d - \mathbf{1}_t\mathbf{1}_t'$ 

We will denote the matrix  $T_dQ_BL_d$  by  $K_d$ .

Observing, that  $\mathbf{E}_t$  is an idempotent matrix, i.e.  $\mathbf{E}_t \mathbf{E}_t = \mathbf{E}_t$ , and according to (3), we get

$$\mathbf{C}_d = t\mathbf{E}_t - \frac{1}{t}\mathbf{K}_d\mathbf{K}_d'. \tag{4}$$

Denote elements of the matrix  $\mathbf{T}_d^i\mathbf{L}_d$  by  $l_{dij}$ ,  $1 \le i, j \le t$ . Since each  $l_{dij}$  is the number of occurrences of treatment i with treatment j as left neighbor, it has a value from the set  $\{0,1,...,t\}$ , with  $l_{dii}=0$  for binary designs. This implies that for a design  $d \in \mathcal{D}_t$ , the matrix  $\mathbf{K}_d$  belongs to the class  $K_{(t)}$  defined as follows:

$$K_{(t)} = \{ \mathbf{K}_d = (k_{ij}) \in \mathbf{Z}^{t \times t} : \mathbf{K}_d \mathbf{1}_t = \mathbf{K}_d' \mathbf{1}_t = \mathbf{0}_t, k_{ij} \in \{-1, 0, 1, ..., t - 1\},$$
$$k_{ii} = -1, 1 \le i, j \le t \},$$

where  $Z^{t\times t}$  is the set of all  $t\times t$  integer matrices.

The matrix  $\mathbf{T}_d'\mathbf{L}_d$  is called a *left-neighbor matrix* of design d and can be presented as

$$\mathbf{T}_d' \mathbf{L}_d = \mathbf{K}_d + \mathbf{1}_t \mathbf{1}_t'. \tag{5}$$

# 4. E-optimal designs

In this section we give the structure of the left-neighbor matrix of design  $d^* \in \mathcal{D}_t$ , which is E-optimal over the class  $\mathcal{D}_t$ ,  $t \ge 2$ . We give the methods of construction of the E-optimal designs over  $\mathcal{D}_t$ , for  $3 \le t \le 10$ . Since the information matrix and the left-neighbor matrix of design d can be expressed as a function of the matrix  $K_d$  (see (4) and (5)), which has row and column sums zero, the results will be given in terms of  $K_d$ .

For a design  $d \in \mathcal{D}_{t,b,k}$  let  $0 = \mu_0(\mathbf{C}_d) \le \mu_1(\mathbf{C}_d) \le ... \le \mu_{t-1}(\mathbf{C}_d)$  be the eigenvalues of its information matrix  $\mathbf{C}_d$ . A design  $d^* \in \mathcal{D}_{t,b,k}$  is called *E-optimal*, if  $\mu_1(\mathbf{C}_{d^*}) \ge \mu_1(\mathbf{C}_d)$  for all designs  $d \in \mathcal{D}_{t,b,k}$  (Constantine, 1981).

Observe that for design  $d \in \mathcal{D}_t$ , the matrices  $\mathbf{E}_t$  and  $\mathbf{K}_d \mathbf{K}_d'$  in (4) commute. Thus we are interested in determining the structure of the matrix  $\mathbf{K}_d$ , for which the largest eigenvalue of  $\mathbf{K}_d \mathbf{K}_d'$  is minimal over all matrices from  $K_{(t)}$ , i.e. such structure of the matrix  $\mathbf{K}_d$  that

$$\mu_{t-1}(\mathbf{K}_{d} \cdot \mathbf{K}_{d'}') = \min_{d \in \mathcal{D}_{t}} \mu_{t-1}(\mathbf{K}_{d} \mathbf{K}_{d}').$$

Let  $\widetilde{\mathbf{H}}_n$  denote a matrix permutationally similar to  $\mathbf{H}_n$ , i.e.  $\widetilde{\mathbf{H}}_n = \mathbf{P}\mathbf{H}_n\mathbf{P}'$  for an arbitrary matrix  $\mathbf{P} \in \mathcal{P}_n$ , where  $\mathcal{P}_n$  is the set of  $n \times n$  permutation matrices. The proof of the following theorem, which is a basis for construction of E-optimal designs, can be found in Filipiak et al. (2005).

**Theorem 1.** Let design  $d^*$  be an E-optimal design in the class  $\mathcal{D}_l$ . Then

- (i) for t = 2,3,5,7:  $\mathbf{K}_{d'} = \widetilde{\mathbf{H}}_{t} \mathbf{I}_{t}$ ;
- (ii) for t = 4:  $\mathbf{K}_{d^*} = (\mathbf{I}_2 \otimes \widetilde{\mathbf{H}}_2) \mathbf{I}_4$ ;
- (iii) for  $t \in \mathbb{N}$ ,  $t \ge 8$  there exist  $i, j \in \mathbb{N} \cup \{0\}$  such that t = 3i + 5j and

$$\mathbf{K}_{d'} = \begin{cases} \mathbf{I}_{m} \otimes (\widetilde{\mathbf{H}}_{3} - \mathbf{I}_{3}) & \text{if } t = 3m, \\ \operatorname{diag}(\mathbf{I}_{i} \otimes (\widetilde{\mathbf{H}}_{3} - \mathbf{I}_{3}), \mathbf{I}_{j} \otimes (\widetilde{\mathbf{H}}_{5} - \mathbf{I}_{5})), & \text{if } t \neq 3m, \end{cases} m \in \mathbb{N}.$$

From this theorem it follows that the left-neighbor matrix of an E-optimal design has zero diagonal, exactly one off-diagonal element equal to 2 in each row and column, and the remaining off-diagonal elements are equal to 1. This implies that an

E-optimal design must have two class of ordered pairs of neighboring treatments: t(t-2) pairs which occur exactly once in a design and t ordered pairs which occur exactly twice in a design. The main problem in the construction of E-optimal designs is which pairs occur once and which twice.

From the form of the matrix  $T_d$  we can observe that each block of complete binary design is represented by a one-cycle permutation matrix. Thus, if we decompose the left-neighbor matrix to the sum of t one-cycle permutation matrices, we obtain a design. Recall that each permutation is a cycle or a product of disjoint cycles (see e.g. Birkhoff and Mac Lane, 1954). For example, the matrix  $H'_3$  is a one-cycle permutation matrix, which presents the cycle:  $1 \rightarrow 2, 2 \rightarrow 3, 3 \rightarrow 1$  (indexes of elements equal to 1). Observe that, if we write this cycle in the form [123], we can regard it as a treatment sequence in a simple block of design. Thus, if we express the left-neighbor matrix of design d as the sum of t one-cycle permutation matrices, we obtain the treatment sequences of each block of design d.

From Theorem 1 it follows that for different t we have different forms of the matrix  $\mathbf{K}_{d^*}$ . In consequence, to construct E-optimal designs we must use different methods for different values of t. Thus we give some hints on how to decompose left-neighbor matrices of E-optimal designs over  $\mathcal{D}_t$  in accordance with the results of Theorem 1.

**Case 1.** Let t = 3,5 or 7. By Theorem 1 (i) and according to (5), the left-neighbor matrix of E-optimal design  $d^*$  is permutationally similar to the matrix  $\mathbf{H}_t - \mathbf{I}_t + \mathbf{1}_t \mathbf{1}_t$ . This matrix can be written as the sum of t matrices, which are j th powers of  $\mathbf{H}_t$ ,  $j \neq t$ . Then we have the following examples of E-optimal designs:

for 
$$t = 3$$
:

for 
$$t = 5$$
:

$$d^* = \begin{pmatrix} 2 & 1 & 3 & 2 \\ 3 & 1 & 2 & 3 \\ 2 & 1 & 3 & 2 \end{pmatrix},$$

$$d^{\bullet} = \begin{pmatrix} 2 & 1 & 5 & 4 & 3 & 2 \\ 5 & 1 & 2 & 3 & 4 & 5 \\ 4 & 1 & 3 & 5 & 2 & 4 \\ 3 & 1 & 4 & 2 & 5 & 3 \\ 2 & 1 & 5 & 4 & 3 & 2 \end{pmatrix}$$

and for t = 7:

$$d^* = \begin{pmatrix} 2 & 1 & 7 & 6 & 5 & 4 & 3 & 2 \\ 3 & 1 & 6 & 4 & 2 & 7 & 5 & 3 \\ 4 & 1 & 5 & 2 & 6 & 3 & 7 & 4 \\ 5 & 1 & 4 & 7 & 3 & 6 & 2 & 5 \\ 6 & 1 & 3 & 5 & 7 & 2 & 4 & 6 \\ 7 & 1 & 2 & 3 & 4 & 5 & 6 & 7 \\ 2 & 1 & 7 & 6 & 5 & 4 & 3 & 2 \end{pmatrix}.$$

Observe that, if we delete the last block from each of these designs, we obtain circular neighbor balanced designs (see e.g. Druilhet, 1999) which are universally optimal over the class  $\mathcal{D}_{t,b,k}$  (if they exist). Filipiak and Różański (2004) showed that circular neighbor balanced designs with one block repeated, i.e. designs  $d^*$ , are highly efficient over  $\mathcal{D}_t$ .

Case 2. Let t = 4. By Theorem 1 (ii) and according to (5), the left-neighbor matrix of E-optimal design  $d^*$  is permutationally similar to the matrix  $(\mathbf{I}_2 \otimes \mathbf{H}_2) - \mathbf{I}_4 + \mathbf{1}_4 \mathbf{I}_4'$ . Thus an example of an E-optimal design over  $\mathcal{D}_4$  is

$$d^* = \begin{pmatrix} 2 & 1 & 4 & 3 & 2 \\ 4 & 1 & 2 & 3 & 4 \\ 3 & 1 & 2 & 4 & 3 \\ 2 & 1 & 3 & 4 & 2 \end{pmatrix}.$$

Observe that the number of one-cycle permutation matrices increases rapidly with t. To reduce the number of possible decompositions, we can consider block forms of permutation matrices, which follows from the block-diagonal forms of the matrix  $\mathbf{K}_{d}$  in Theorem 1 (iii). To illustrate (iii) we give examples of the construction of the E-optimal designs for t = 6, t = 9, and t = 8, t = 10.

Before we present the basis of the method of construction of the E-optimal design for mentioned t, we introduce the following notation:  $\Theta_{n \times m}$  denotes the  $n \times m$  matrix of zeros,  $\Delta_n = (\delta_{ij})$  is the  $n \times n$  matrix with  $\delta_{ij} = 1$  if j = n + 1 - i and zero otherwise,  $1 \le i, j \le n$ , and the  $n \times n$  matrix of zeros we denote in short by  $\Theta_n$ .

Case 3. Let t = 3m,  $m \in \{2,3\}$ . The left-neighbor matrix of the E-optimal design is given by (5) and Theorem 1 (iii).

a) Let t=6. We obtain the E-optimal design over  $\mathcal{D}_6$  if we decompose the left-neighbor matrix to the sum of three matrices permutationally similar to  $\mathbf{U}_6$  and three matrices permutationally similar to  $\mathbf{V}_6$ , where

$$\mathbf{U}_6 = \begin{pmatrix} \mathbf{P} & \mathbf{\Theta}_3 \\ \mathbf{\Theta}_3 & \mathbf{Q} \end{pmatrix} \mathbf{H}_6' \begin{pmatrix} \mathbf{P}' & \mathbf{\Theta}_3 \\ \mathbf{\Theta}_3 & \mathbf{Q}' \end{pmatrix},$$

$$\mathbf{V}_6 = \begin{pmatrix} \mathbf{R} & \Theta_3 \\ \Theta_3 & \mathbf{S} \end{pmatrix} \begin{pmatrix} \Theta_{4\times 2} & \mathbf{I}_4 \\ \Delta_2 & \Theta_{2\times 4} \end{pmatrix} \begin{pmatrix} \mathbf{R}' & \Theta_3 \\ \Theta_3 & \mathbf{S}' \end{pmatrix}$$

and  $P,Q,R,S \in \mathcal{P}_3$ .

An example of E-optimal design is:

$$d^* = \begin{pmatrix} 6 & 1 & 2 & 3 & 4 & 5 & 6 \\ 3 & 1 & 2 & 4 & 6 & 5 & 3 \\ 4 & 1 & 3 & 2 & 5 & 6 & 4 \\ 3 & 1 & 4 & 5 & 2 & 6 & 3 \\ 2 & 1 & 5 & 4 & 3 & 6 & 2 \\ 5 & 1 & 6 & 4 & 2 & 3 & 5 \end{pmatrix}.$$

b) Let t = 9. We obtain the E-optimal design over  $\mathcal{D}_9$  if we write the left-neighbor matrix as the sum of three matrices permutationally similar to  $\mathbf{U}_9$ , three matrices permutationally similar to  $\mathbf{V}_9$ , and three matrices permutationally similar to  $\mathbf{Z}_9$ , where

$$\mathbf{U}_9 = \begin{pmatrix} \mathbf{D} & \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \mathbf{E} & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 & \mathbf{F} \end{pmatrix} \mathbf{H}_9' \begin{pmatrix} \mathbf{D}' & \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \mathbf{E}' & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 & \mathbf{F}' \end{pmatrix},$$

$$\mathbf{V}_9 = \begin{pmatrix} \mathbf{M} & \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \mathbf{N} & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 & \mathbf{P} \end{pmatrix} \begin{pmatrix} \boldsymbol{\Theta}_{2\times7} & \mathbf{I}_7 \\ \mathbf{I}_2 & \boldsymbol{\Theta}_{2\times7} \end{pmatrix} \begin{pmatrix} \mathbf{M}' & \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \mathbf{N}' & \boldsymbol{\Theta}_3 \\ \boldsymbol{\Theta}_3 & \boldsymbol{\Theta}_3 & \mathbf{P}' \end{pmatrix},$$

$$\mathbf{Z}_9 = \begin{pmatrix} \mathbf{Q} & \Theta_3 & \Theta_3 \\ \Theta_3 & \mathbf{R} & \Theta_3 \\ \Theta_3 & \Theta_3 & \mathbf{S} \end{pmatrix} \begin{pmatrix} \Theta_{6\times3} & \mathbf{I}_6 \\ \mathbf{I}_3 & \Theta_{3\times6} \end{pmatrix} \begin{pmatrix} \mathbf{Q}' & \Theta_3 & \Theta_3 \\ \Theta_3 & \mathbf{R}' & \Theta_3 \\ \Theta_3 & \Theta_3 & \mathbf{S}' \end{pmatrix}$$

and  $D, E, F, M, N, P, Q, R, S \in \mathcal{P}_3$ .

Case 4. Let  $t \ge 8$  and  $t \ne 3m$ ,  $m \in \mathbb{N}$ . The left-neighbor matrix of the E-optimal design is given by (5) and Theorem 1 (iii).

a) Let t=8. We obtain the E-optimal design over  $\mathcal{D}_8$  if we decompose the left-neighbor matrix to the sum of three matrices permutationally similar to  $U_8$ , three matrices permutationally similar to  $V_8$ , and two matrices permutationally similar to  $Z_8$ , where:

$$\mathbf{U}_{8} = \begin{pmatrix} \mathbf{D} & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{P} \end{pmatrix} \mathbf{H}_{8}^{'} \begin{pmatrix} \mathbf{D}' & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{P}' \end{pmatrix},$$

$$\mathbf{V}_8 = \begin{pmatrix} \mathbf{E} & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{Q} \end{pmatrix} \begin{pmatrix} \Theta_{6\times2} & \mathbf{I}_6 \\ \Delta_2 & \Theta_{2\times6} \end{pmatrix} \begin{pmatrix} \mathbf{E}' & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{Q}' \end{pmatrix},$$

$$\mathbf{Z}_{8} = \begin{pmatrix} \mathbf{F} & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{R} \end{pmatrix} \begin{pmatrix} \Theta_{5\times3} & \mathbf{I}_{5} \\ \mathbf{H}_{3} & \Theta_{3\times5} \end{pmatrix} \begin{pmatrix} \mathbf{F}' & \Theta_{3\times5} \\ \Theta_{5\times3} & \mathbf{R}' \end{pmatrix}$$

and  $\mathbf{D}, \mathbf{E}, \mathbf{F} \in \mathcal{P}_3$ ,  $\mathbf{P}, \mathbf{Q}, \mathbf{R} \in \mathcal{P}_5$ .

b) Let t = 10. We obtain the E-optimal design over  $\mathcal{D}_{10}$  if we write the left-neighbor matrix as the sum of five matrices permutationally similar to  $\mathbf{U}_{10}$  and five matrices permutationally similar to  $\mathbf{V}_{10}$ , where:

$$\mathbf{U}_{10} = \begin{pmatrix} \mathbf{P} & \Theta_5 \\ \Theta_5 & \mathbf{Q} \end{pmatrix} \mathbf{H}_{10}' \begin{pmatrix} \mathbf{P}' & \Theta_5 \\ \Theta_5 & \mathbf{Q}' \end{pmatrix},$$

$$\mathbf{V}_{10} = \begin{pmatrix} \mathbf{R} & \Theta_5 \\ \Theta_5 & \mathbf{S} \end{pmatrix} \begin{pmatrix} \Theta_{6\times4} & \mathbf{I}_6 \\ \mathbf{H}_4 & \Theta_{4\times6} \end{pmatrix} \begin{pmatrix} \mathbf{R'} & \Theta_5 \\ \Theta_5 & \mathbf{S'} \end{pmatrix}$$

and  $P,Q,R,S \in \mathcal{P}_5$ .

Observe, that the decomposition of the matrix  $\mathbf{T}_d' \mathbf{L}_d$  is not unique. Moreover, since we are considering a circular interference model, the information matrix does not depend on the first treatment in a block. Thus the E-optimal designs given in this paper are not determined uniquely. Nevertheless, using decomposition of the left-neighbor matrix of the E-optimal design to the sum of permutation matrices given in Case 1 - Case 4, we can generate all E-optimal designs over  $\mathcal{D}_t$ .

For the interference model with right-neighbor effects, the results given in this paper still hold. This implies that the designs given in this paper are E-optimal under the interference model with left-neighbor effects as well as under the interference model with right-neighbor effects.

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