International Journal of Mathematical Archive-6(9), 2015, 187-192
Available online through www.ijma.info ISSN 2229 – 5046

CONSTRUCTION OF SOME NEW OPTIMAL CROSS-OVER DESIGNS OF FIRST ORDER

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(Received On: 09-09-15; Revised & Accepted On: 30-09-15)

ABSTRACT

In cross-over designs, each experimental unit receives a sequence of treatments over a number of successive periods and the effect of the treatment continues beyond the period of its application. These designs are applied in the field of clinical trials, psychological experiments, consumer research trials and many more. In this paper, we develop some new families of balanced cross-over designs of first order, which are universally optimal.

Keywords: *Direct treatment effects; Residual treatment effects; Initial sequences; Cross-over designs of first order; Universal optimality.*

AMS Subject Classification: *Primary 62K15; Secondary 05B30.*

1. INTRODUCTION

Designs in which each experimental unit receives a sequence of treatments over several periods and the effect of the treatment continues beyond the period of its application are termed as cross-over designs (CODs). CODs have now found applications in many research areas including agricultural sciences, dairy husbandry, bioassay procedures, medical applications, psychological experiments, industrial settings. These designs are extremely useful when the experimental units are scarce. When different treatments are applied to each experimental unit, every treatment will produce two types of effects: direct effects and residual effects. Designs in which the residual effects persist till the following period are the designs of first order while those for which the residual effects persist for two periods after the application of treatments are designs of second order.

Williams (1949, 1950) introduced balanced CODs (especially for first and second orders). Bradley (1958) and Sheehe and Bross (1961) also gave simple methods of construction of balanced CODs of first order. Patterson (1952) developed some balanced CODs for which the number of periods is less than the number of treatments. For an excellent review on CODs, see Hedayat and Afsarinejad (1975), Jones and Kenward (1989), Shah and Sinha (1989), Afsarinejad (1990), and Stufken (1996).

The universal optimality of certain balanced CODs in a certain class of competing designs has been studied by Hedayat and Afsarinejad (1978), Cheng and Wu (1980), Kunnert (1984), Raghavarao and Shah (2001) and Bose and Dey (2009). Dey, Gupta and Singh (1983) have discussed the optimality aspects of CODs when the number of periods is less than the number of treatments.

In this paper, we have constructed some universally optimal balanced CODs of first order. The paper is organised as follows. In Section 2, we give definition and notations. The optimal properties of the designs are discussed in Section 3. In Section 4, we describe the methods of construction of some new balanced CODs.

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2. PRELIMINARY

Let us consider a COD in which v treatments are compared using N experimental units and the experiment lasts for k periods. We have the following conditions, due to Patterson (1952), for a COD to be balanced:

I. No treatment symbol occurs in a given sequence more than once.
II. Each treatment symbol occurs in a given period an equal number of times.
III. Every two treatment symbols occur together in the same number of sequences.
IV. Each ordered succession of two treatment symbols occurs equally often in sequences.
V. Every two treatment symbols occur together in the same number of curtailed sequences formed by omitting the final period.
VI. In those sequences in which a given treatment occurs in the final period the other treatments occur equally often.
VII. In those sequences in which a given treatment occurs in any but the final period each other treatment occurs equally often in the final period.

The numbers v, N and k are the parameters of a COD of first order.

3. MODEL AND OPTIMALITY

Let us consider a COD of first order in which v treatments are compared using N experimental units and the experiment lasts for k periods. Let $\zeta = \zeta\,(v, N, k)$ denote the class of all such CODs. A commonly assumed linear model for the analysis is

$$y_{ij} = \mu + \alpha_i + \beta_j + \tau_{d(i,j)} + \rho_{d(i-1,j)} + e_{ij} \tag{3.1}$$

where y_{ij} $(1 \le i \le k;\ 1 \le j \le N)$ is the response observed in the i^{th} period on the j^{th} unit, μ the general mean, α_i the i^{th} period effect, β_j the j^{th} unit effect, $\tau_{d(i,j)}$ the direct effect of the treatment d(i,j), $\rho_{d(i-1,j)}$ the first order residual effect of the treatment d(i,j) with $\rho_{d(0,j)} = 0$ for all j, e_{ij} are random errors assumed to be normally and independently distributed with mean zero and variance σ^2. All the parameters in (3.1) are assumed to be fixed.

In matrix notations, the model (3.1) can be written as

$$\mathbf{Y} = \mu\mathbf{1} + \mathbf{P}\boldsymbol{\alpha} + \mathbf{U}\boldsymbol{\beta} + \mathbf{D}\boldsymbol{\tau} + \mathbf{R}\boldsymbol{\eta} + \boldsymbol{\varepsilon} \tag{3.2}$$

where, $\mathbf{Y}$ is an $Nk \times 1$ vector of observations; μ is the general mean; $\boldsymbol{\alpha}$ is the $k \times 1$ vector of period effects; $\boldsymbol{\beta}$ is the $N \times 1$ vector of unit effects; $\boldsymbol{\tau}$ is a $v \times 1$ vector of direct effects of treatments; $\boldsymbol{\eta}$ is a $v \times 1$ vector of first order residual effects of treatments; $\mathbf{D}$ is an $Nk \times v$ incidence matrix of observations vs direct effects; $\mathbf{R}$ is an $Nk \times v$ incidence matrix of observations vs residual effects; $\mathbf{P}$ is an $Nk \times k$ incidence matrix of observations vs periods; $\mathbf{U}$ is an $Nk \times N$ incidence matrix of observations vs units; $\mathbf{1}_t$ is a $t \times 1$ vector of ones.

We also define the following matrices:

$\mathbf{M} = \mathbf{D}'\mathbf{R}$ is $v \times v$ incidence matrix of direct effects vs first residual effects; $\mathbf{L}_1 = \mathbf{D}'\mathbf{P}$ is $v \times k$ incidence matrix of direct effects vs periods; $\mathbf{E} = \mathbf{R}'\mathbf{P}$ is $v \times k$ incidence matrix of residual effects vs periods; $\mathbf{L}_2 = \mathbf{D}'\mathbf{U}$ is $v \times N$ incidence matrix of direct effects vs units; $\mathbf{N}_1 = \mathbf{R}'\mathbf{U}$ is $v \times N$ incidence matrix of residual effects vs units.

We also have $\mathbf{D}'\mathbf{1} = \mathbf{r}$ a $v \times 1$ vector of replication of direct effects; $\mathbf{R}'\mathbf{1} = \boldsymbol{\rho}$ a $v \times 1$ vector of replication of residual effects; $\mathbf{D}'\mathbf{D} = \mathbf{r}^{\delta} = \mathrm{diag}(r_1, r_2, \cdots, r_v)$; $\mathbf{R}'\mathbf{R} = \boldsymbol{\rho}^{\delta} = \mathrm{diag}(\rho_1, \rho_2, \cdots, \rho_v)$.

We now have the following lemma, whose proof is straight forward:

Lemma 3.1: The joint information matrix of the direct effects and first order residual effects is given by

$$C_d(\boldsymbol{\tau}, \boldsymbol{\rho}) = \begin{bmatrix} \mathbf{C}_{11} & \mathbf{C}_{12} \\ \mathbf{C}_{21} & \mathbf{C}_{22} \end{bmatrix} \tag{3.3}$$

where, $\mathbf{C}_{11} = \mathbf{r}^{\delta} - \frac{1}{N}\mathbf{L}_1\mathbf{L}_1' - \frac{1}{k}\mathbf{L}_2\mathbf{L}_2' + \frac{1}{Nk}\mathbf{r}\mathbf{r}'$, $\mathbf{C}_{12} = \mathbf{M} - \boldsymbol{\rho}\frac{1}{N}\mathbf{L}_1 E' - \frac{1}{k}\mathbf{L}_2\mathbf{N}_1' + \frac{1}{Nk}\mathbf{r}\ '$, $\mathbf{C}_{21} = \mathbf{C}_{12}'$,

$$\mathbf{C}_{22} = \boldsymbol{\rho}^{\delta} - \frac{1}{N}\mathbf{E}\mathbf{E}' - \frac{1}{k}\mathbf{N}_1\mathbf{N}_1' + \frac{1}{Nk}\boldsymbol{\rho}\boldsymbol{\rho}'.$$

In the search for optimal CODs, we make an appeal to the concept of universal optimality given by Kiefer (1975). If a design d^* is universally optimal, then it is D-, A-, and E-optimal. First we need the following definition.

Definition 3.1: A design d is said to be completely symmetric with respect to θ_1 if its corresponding $\mathbf{C}_d$ is of the form $a\mathbf{I} + b\mathbf{11}'$, where a and b are scalars, $\mathbf{I}_v$ is the identity matrix of order v and $\mathbf{1}_v$ is a v-component vector of ones.

Theorem 3.1: (Kiefer, 1975). If the class of competing designs **D** contains a design d^* such that

1. d^* is completely symmetric,
2. trace ($\mathbf{C}_{d^*}$) > trace ($\mathbf{C}_d$) for all d such that $\mathbf{C}_d \,\varepsilon\, \mathbf{R}_v$, then d^* is universally optimum, where $\mathbf{R}_v$ denotes the class of all symmetric, non-negative matrices of order v with row sums equal to zero.

Dey *et al.* (1983) gave the following conditions for the class of competing designs to search for a universally optimal COD:

(i) No treatment symbol occurs in a given sequence more than once.
(ii) Each treatment symbol occurs in a given period an equal number of times.
(iii) Every pair of treatments occurs together in the same number of sequences.
(iv) Every pair of treatments occurs together in the same number of curtailed sequences formed by omitting the final period.

The conditions characterizing the class of designs Ω form a subset of the conditions required for a balanced COD. However, every member of Ω is not balanced.

Now we have the following theorems due to Dey *et al.* (1983):

Theorem 3.2: A design d^* in Ω is universally optimal for the estimation of direct effects if $\mathbf{M}_{d^*} = \lambda\left(\mathbf{1}_v\mathbf{1}_v' - \mathbf{I}_v\right)$, where λ is a scalar.

Theorem 3.3: A design d^* in Ω is universally optimal for the estimation of residual effects of first order if $\mathbf{M}_{d^*} = \lambda\left(J_{v,v} - \mathbf{I}_v\right)$, where λ is a scalar.

It is, therefore, obvious that the universally optimal COD in Ω is necessarily a balanced COD.

4. CONSTRUCTION OF BALANCED CODs

We now describe construction of some families of universally optimal balanced CODs of first order.

Family 1: Let $v = 4m + 1$ be a prime or a prime power and let x be a primitive element of GF(v). Consider a BIBD with the parameters $v = 4m+1$, $b = 2(4m+1)$, $r = 4m$, $k = 2m$, $\lambda = 2m-1$ and with the initial blocks $I_1 = \left(x^0 \quad x^2 \quad x^4 \quad \cdots \quad x^{4m-2}\right)$ and
$I_2 = \left(x \quad x^3 \quad x^5 \quad \cdots \quad x^{4m-1}\right)$.

We now construct a universally optimal balanced COD of first order as follows:

1. Choose any one block of the above initial blocks.
2. Obtain the (v - 1) initial sequences from the above block by multiplying with every non-zero element of GF(v).
3. By developing the initial sequences mod (v), we get a universally optimal balanced COD of first order with parameters $v = 4m+1$, $N = 4m(4m+1)$, $k = 2m$.

We explain the method with the help of an example.

Example 4.1: For v = 13, $x = 2$ is a primitive element of GF(13). Then there exists a BIBD with the two initial blocks
(1 4 3 12 9 10) and (2 8 6 11 5 7).

We consider the first initial block (1 4 3 12 9 10). Then twelve initial sequences will be

1	2	3	4	5	6	7	8	9	10	11	12
4	8	12	3	7	11	2	6	10	1	5	9
3	6	9	12	2	5	8	11	1	4	7	10
12	11	10	9	8	7	6	5	4	3	2	1
9	5	1	10	6	2	11	7	3	12	8	4
10	7	4	1	11	8	5	2	12	9	6	3.

By developing the above initial sequences mod 13, we get a universally optimal balanced COD of first order with parameters

v = 13, N = 156, k = 6.

Family 2: Let $v = 6m + 1$ be a prime or a prime power and let x be a primitive element of GF(v). Consider the set of m initial blocks

$$I_i = \left(x^{i-1} \quad x^{2m+i-1} \quad x^{4m+i-1}\right), i = 1, 2, \cdots, m$$

Every non-zero element of GF(v) should occur the same number of times in the set $(I_i, -I_i)$, where the set $-I_i$ is the additive inverses of the elements of I_i.

By adding the treatment 0 to the chosen block and using the steps as discussed for Family 1 resulting in a universally optimal balanced COD of first order with parameters $v = 6m + 1$, $N = 6m(6m + 1)$, $k = 4$.

We illustrate the method through an example.

Example 4.2: For v = 7, we choose the block (1 2 4). Add the treatment 0 to this block. Then by multiplying with every non-zero element of GF(7) we obtain the following six initial sequences

0 0 0 0 0 0
1 2 3 4 5 6
2 4 6 1 3 5
4 1 5 2 6 3.

By developing the above six initial sequences mod 7, we get a universally optimal balanced COD of first order with parameters

v = 7, N = 42, k = 4.

Family 3: Let $v = 2m + 1$ be an odd prime, or an odd prime power and let x be a primitive element of GF(v). Consider a balanced ternary design, given by Saha and Dey (1973), with the initial block $\left(0 \quad x^0 \quad x^0 \quad x^2 \quad x^2 \quad x^4 \quad x^4 \quad \cdots \quad x^{2m-2} \quad x^{2m-2}\right)$; m being a positive integer, and with the parameters $v = 2m + 1 = b = r = k$, $\mu = 2m$.

A universally optimal balanced COD of first order with parameters $v = 2m + 1$, $N = 2m(2m+1)$, $k = m + 1$ is obtained by considering the block of the given design with distinct treatments i.e., $\left(0 \quad x^0 \quad x^2 \quad \cdots \quad x^{2m-2}\right)$ at the step 1 and using the other steps discussed for Family 1.

We explain the method with the help of an example.

Example 4.3: For v = 5, we consider the block with distinct treatments (0 1 4). Then by multiplying with every non-zero element of GF(5) we obtain the following four initial sequences

0 0 0 0
1 2 3 4
4 3 2 1.

By developing the above four initial sequences mod 5, we get a universally optimal balanced COD of first order with parameters

v = 5, N = 20, k = 3.

Family 4: Consider a balanced n-ary design, given by Shah and Gujarathi (1989), with parameters v^*, b^*, r^*, k^*, π^*, based on a set of mutually orthogonal Latin squares (MOLS).

By obtaining a new block, from the chosen block, with all the distinct treatments and using the steps as discussed for Family 1 results in a universally optimal balanced COD of first order with parameters $v = v^*$, $N = v^*(v^* - 1)$, k .

We illustrate the method through an example.

Example 4.4: For v = 5, there exists a balanced 4-ary design with the parameters

V* = 5, B* = 20, R* = 32, K* = 8, π* = 46

and with the blocks
(0 1 1 3 3 4 4 4), (0 0 2 2 2 3 4 4), (1 1 1 2 2 3 3 4), (0 0 1 2 2 3 3 3), (0 0 0 1 1 2 4 4),
(0 2 2 3 3 3 4 4), (0 0 1 1 1 2 3 3), (1 1 2 2 3 4 4 4), (0 0 1 1 2 2 2 4), (0 0 0 1 3 3 4 4),
(0 1 1 2 2 2 3 3), (0 0 1 2 2 4 4 4), (1 1 2 3 3 3 4 4), (0 0 1 1 1 3 4 4), (0 0 0 2 2 3 3 4),
(0 1 1 1 2 2 4 4), (0 0 1 1 3 3 3 4), (1 2 2 2 3 3 4 4), (0 0 2 3 3 4 4 4), (0 0 0 1 1 2 2 3).

We consider the block (0 0 0 1 3 3 4 4). The new block with all distinct treatments is given by

(0 1 3 4)

Then the four initial sequences will be

0	0	0	0
1	2	3	4
3	1	4	2
4	3	2	1

By developing the above initial sequences mod 5, we get a universally optimal balanced COD of first order

v = 5, N = 20, k = 4.

Family 5: Let v be an odd prime power. Consider the initial blocks of an ${}^{N}C_{m}$ - type PBIB design, given by Saha et al. (1973), with the parameters of the second kind v, $b = sv/2$, $r = sk/2$, k, λ_i ; $n_i = s = (v - 1)/m$, $1 \leq i \leq m$.

A universally optimal balanced COD of first order with parameters v, $N = v(v - 1)$, k is obtained similarly along the lines of Family 1.

We explain the method with the help of an example.

Example 4.5: For v = 13, there exists an ${}^{N}C_{m}$ – type PBIB design with the parameters

$$v = 13,\ b = 39,\ r = 9,\ k = 3,\ \lambda_1 = 2,\ \lambda_2 = 1;\quad n_1 = n_2 = s = 6,$$

and with the initial blocks

(1 2 4), (4 8 3), (3 6 12).

We choose the block (1 2 4). Then by multiplying with every non-zero element of GF(13) we obtain the following twelve initial sequences

1	2	3	4	5	6	7	8	9	10	11	12
2	4	6	8	10	12	1	3	5	7	9	11
4	8	12	3	7	11	2	6	10	1	5	9.

By developing the above initial sequences mod 13, we get a universally optimal balanced COD of first order with parameters

v = 13, N = 156, k = 3.

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Source of support: Nil, Conflict of interest: None Declared