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Block designs with nested rows and columns for symmetric parallel line assays

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Summary

Symmetric parallel lines bioassays with even number of doses of each preparation are considered when a block design with nested rows and columns is used for the experiment. Thus, it is assumed that two sources of nuisance variability are to be controlled in the experiment. Nested row-column designs which estimate the preparation contrast, the combined regression contrast and the parallelism contrast with full efficiency are characterized and some methods of construction are provided.

1 Introduction

Suppose that a symmetric parallel line (SPL) assay involving two preparations, standard and test, each at m equi-spaced doses is to be conducted using a block design with nested rows and columns. Singh and Dey (1979) defined variance balanced incomplete block designs with nested rows and columns. Since then several authors have given methods of constructing variance balanced and partially variance balanced designs with nested rows and columns, e.g. Agrawal and Prasad (1982, 1983), Sreenath (1989), Uddin and

Morgan (1990). The purpose of this paper is to consider these designs for SPL assays when m, the number of doses of each preparation, is even.

The preparation contrast L_p, the combined regression contrast L_1, and the parallelism contrast L_1^1 are of main importance in SPL assays. The L_p and L_1 provide an estimate of relative potency and L_1^1 is important for testing deviation from parallelism of the regression lines for the standard and the test preparations. Therefore it is desired to estimate these three contrasts with full efficiency. Designs which estimate L_p, L_1 and L_1^1 with full efficiency will be referred to as L-designs in this paper.

L-designs with one dimensional blocks have been considered by several authors, see for example Kyi Win and Dey (1980), Nigam and Boopathy (1985), Gupta (1989), Gupta and Mukerjee (1991). Das and Kulkarni (1966) gave some designs which estimate L_p and L_1 with full efficiency. The reader is referred to Kshirsagar and Yuan (1992) for a unified theory of parallel line bioassays in incomplete block designs.

L-designs with nested rows and columns are defined in Section 2. Then some characterization and construction aspects are considered in Section 3.

2 L-designs with nested rows and columns

Let $s_1 < s_2 < \cdots < s_u < s_{u+1} < \cdots < s_m$ and $t_1 < t_2 < \cdots < t_u < t_{u+1} < \cdots < t_m$, where $m = 2u$, denote the doses of the standard and the test preparations respectively. Let these $v = 2m$ treatments be coded as $1, 2, \cdots, 2m$ respectively. Also, let $\tau = (\tau_1 \ \tau_2 \cdots \tau_v)'$ be the vector of treatment parameters where τ_i and τ_{m+i} denote the effects of s_i and t_i respectively, $i = 1, 2, \cdots, m$. Let $e_i, i = 1, 2, \cdots, m-1$, denote all possible contrast vectors of size m as given by orthogonal polynomials. Let

$$\begin{aligned} \ell_p &= (1'_m \quad -1'_m)' \qquad (2.1) \\ \ell_{i1} &= (e'_i \quad e'_i)', \;\; l_{i2} = (e'_i \quad -e'_i)', \;\; i = 1, 2, \cdots, m-1, \end{aligned}$$

where 1_q denotes a column vector of $1'$s of size q. Then

$$\begin{aligned} L_p &= \ell_p' \tau, \\ L_i &= \ell_{i1}' \tau, \quad L_i^1 = \ell_{i2}' \tau, \quad i = 1, 2, \cdots, m-1. \end{aligned} \tag{2.2}$$

It should be noted that $e_i, i = 1, 2, \cdots, m-1$, have the following structure,

$$e_i' = \begin{cases} f_i' \; [I_u \quad -I_{cu}] \;, & i = 1, 3, 5, \cdots, m-1 \\ \\ f_i' \; [I_u \quad I_{cu}] \;, & i = 2, 4, 6, \cdots, m-2 \end{cases} \tag{2.3}$$

where $f_i = [f_{i1} \; f_{i2} \; \cdots \; f_{iu}]'$ is a column vector of size u, $i = 1, 2, \cdots, m-1$, I_u is the identity matrix and I_{cu} denotes the matrix containing unity in the $(i, u+1-i)$ positions, $i = 1, 2, \cdots, u$, and zero elsewhere, both being of order $u \times u$. Since $e_i'1 = e_i'e_j = 0$, using (2.3) it follows that $f_i'1_u = f_i'f_j = 0$, $i \neq j = 2, 4, 6, \cdots, m-2$.

First consider a SPL assay conducted using an incomplete block design having b blocks of k plots each, with every treatment replicated a constant number of times denoted by r. Then, following Kyi Win and Dey (1980) and Gupta (1989), it can be proved that L_p, L_i and $L_i^1, i = 1, 3, 5, \cdots, m-1$, are estimated with full efficiency if the design satisfies the following conditions:

(a) The total number of concurrences of each of the pairs of treatments $(g, m+1-g)$, $(m+g, 2m+1-g), g = 1, 2, \cdots, u$, is equal to r.

(b) Each block of the design contains $k/2$ treatments belonging to $\{1, 2, \cdots, m\}$ where k is necessarily even.

Let us now consider the case of block designs with nested rows and columns for SPL assays. Thus, let each block be arranged in p rows and q columns with $k = pq$. Let N_1, N_2 and N denote the $v \times pb$ treatment versus row, $v \times qb$ treatment versus column, and $v \times b$ treatment versus blocks incidence matrices respectively. The component designs corresponding to N_1, N_2, N will be denoted by D_1, D_2 and D respectively. The reduced normal equations for estimating the vector of treatment parameters are then given by $C\tau = Q$ where

$$C = rI_v - \frac{1}{q}N_1N_1' - \frac{1}{p}N_2N_2' + \frac{1}{pq}NN', \tag{2.4}$$

and Q is the vector of adjusted treatment totals. Along the lines of a L-design with one dimensional blocks considered above, we have the following definition for the case of designs with nested rows and columns.

Definition 2.1. A design with nested rows and columns is defined to be a L-design if it satisfies the following conditions,

(a) the two treatments $g+(j-1)m$ and $mj+1-g$ do not fall in different blocks of either of the two component designs D_1 or $D_2, j = 1,2; g = 1,2,\cdots,u$, and

(b) each of the blocks of the component designs D_1 and D_2 contains an equal number of treatments belonging to $\{1,2,\cdots,m\}$ and $\{m+1, m+2,\cdots,2m\}$, where both p,q are necessarily even.

Using (2.1), (2.3) and (2.4), it can be verified that L-designs with nested rows and columns of Definition 2.1 estimate L_p, L_i and L_i^1 with full efficiency, $i = 1,3,5,\cdots,m-1$.

3 Characterizations and constructions of L-designs

Definition 2.1 implies that a typical block of the component design D_1 or D_2 is of the form,

$$[a_{i(1)} \quad m-a_{i(1)}+1 \quad a_{i(2)} \quad m-a_{i(2)}+1 \quad \cdots \quad a_{i(h)} \quad m-a_{i(h)}+1$$

$$b_{j(1)} \quad 3m-b_{j(1)}+1 \quad b_{j(2)} \quad 3m-b_{j(2)}+1 \quad \cdots \quad b_{j(h)} \quad 3m-b_{j(h)}+1] \tag{3.1}$$

where $4h = q$ if the block belongs to D_1 and $4h = p$ if it belongs to the component design D_2, and

$$
\begin{aligned}
\{a_{i(1)}, a_{i(2)}, \cdots, a_{i(h)}\} &\in \{1, 2, \cdots, u\}, \\
\{b_{j(1)}, b_{j(2)}, \cdots, b_{j(h)}\} &\in \{m+1, m+2, \cdots, m+u\}.
\end{aligned} \tag{3.2}
$$

Each block of D constitutes of p rows and q columns. Consider a typical block of the component design D_1 given by (3.1). The q treatments which are contained in this block belong to q different blocks of the component design D_2. These q blocks of D_2 will be referred to as being associated with that particular block of D_1. from Definition 2.1, if the two treatments $g + (j-1)m$ and $mj + 1 - g$ occur together λ times in some block of the component design D_1, then they must occur together in at least 2λ blocks of D_2 associated with this particular block of D_1. If we now reverse the roles of D_1 and D_2 in the above discussion then it follows that if the pair of treatments $\{g+(j-1)m, mj+1-g\}$ occurs together a certain number of times in the blocks of D_1 associated with a block of D, then it also occurs together the same number of times in the blocks of D_2 associated with that particular block of D. This means that the rows and columns within each block of D can be permuted to yield an arrangement of the following type for each block of D_1 and D_2,

$$
[A_{i(1)}\ A_{i(2)} \cdots A_{i(h)}\ B_{j(1)}\ B_{j(2)} \cdots B_{j(h)}] \tag{3.3}
$$

where

$$
\begin{aligned}
A_{i(\ell)} &= \begin{bmatrix} a_{i(\ell)} & m - a_{i(\ell)} + 1 \\ & \\ m - a_{i(\ell)} + 1 & a_{i(\ell)} \end{bmatrix}, \\
B_{j(\ell)} &= \begin{bmatrix} b_{j(\ell)} & 3m - b_{j(\ell)} + 1 \\ & \\ 3m - b_{j(\ell)} + 1 & b_{j(\ell)} \end{bmatrix},
\end{aligned} \tag{3.4}
$$

$$
\ell = 1, 2, \cdots, h,
$$

and $a_{i(\ell)}$, $b_{j(\ell)}$, $\ell = 1, 2, \cdots, h$, are as defined in equation (3.2). Let

$$A_g = \begin{bmatrix} g & m+1-g \\ m+1-g & g \end{bmatrix}$$

$$B_g = \begin{bmatrix} m+g & 2m+1-g \\ 2m+1-g & m+g \end{bmatrix} = A_g + mJ_2, \quad g = 1, 2, \cdots, u, \tag{3.5}$$

where J_2 is a 2×2 matrix of 1's. Then $A_{i(\ell)}, B_{j(\ell)}$ of equation (3.4) belong to $\{A_1, A_2, \cdots, A_u\}$ and $\{B_1, B_2, \cdots, B_u\}$ respectively.

We now present some methods for obtaining L-designs with nested rows and columns. The case of $q = 2$ will be considered in some detail. Designs for $q \geq 4$ can be derived using designs with $q = 2$. A typical block of a L-design with nested rows and columns having $q = 2$ is given by (3.3). If u is a multiple of h then the blocks,

$$[A_{\ell-1)h+1} \; A_{(\ell-1)h+2} \cdots A_{\ell h} \; B_{(\ell-1)h+1} \; B_{(\ell-1)h+2} \cdots B_{\ell h}]$$
$$\ell = 1, 2, \cdots, w$$

where $w = u/h$, yield a L-design having parameters $v = 2m, b = u/h = w, r = 2, k = 8h, p = 4h, q = 2$. Designs with $q = 2, r = 2$ are necessarily disconnected. For $r = 4$, the following blocks constitute a connected L-design with parameters $v = 2m, b = 2u/h, r = 4, k = 8h, p = 4h, q = 2$,

$$[A_{(\ell-1)h+1} \; A_{(\ell-1)h+2} \cdots A_{\ell h} \; B_{\ell h+1} \; B_{\ell h+2} \cdots B_{(\ell+1)h}],$$

$$\ell = 1, 2, \cdots, w-1,$$

$$[A_{(w-1)h+1}\ A_{(w-1)h+2}\cdots A_{wh}\ B_{(w-1)h+1}\ B_{(w-1)h+2}\cdots B_{wh}],$$

$$[A_{(w-\ell)h+1}\ A_{(w-\ell)h+2}\cdots A_{(w-\ell+1)h}\ B_{(w-\ell-1)h+1}\ B_{(w-\ell-1)h+2}\cdots B_{(w-\ell)h}],$$

$$\ell = 1, 2, \cdots, w-1,$$

$$[A_1\ A_2\ \cdots\ A_h\ B_1\ B_2\ \cdots\ B_h].$$

Example 3.1. Suppose $u = 4, h = 1, r = 4, q = 2$. Then $m = 8$, and using (3.5),

$$A_1 = \begin{bmatrix} 1 & 8 \\ 8 & 1 \end{bmatrix}, A_2 = \begin{bmatrix} 2 & 7 \\ 7 & 2 \end{bmatrix}, A_3 = \begin{bmatrix} 3 & 6 \\ 6 & 3 \end{bmatrix}, A_4 = \begin{bmatrix} 4 & 5 \\ 5 & 4 \end{bmatrix},$$

$$B_g = A_g + 8J_2 \ , \ g = 1, 2, 3, 4.$$

A L-design with nested rows and columns having $v = 16, b = 8, r = 4, k = 8, p = 4$, $q = 2$ is given by

$$[A_1\ B_2],\ [A_2\ B_3],\ [A_3\ B_4],\ [A_4\ B_4],$$

$$[A_4\ B_3],\ [A_3\ B_2],\ [A_2\ B_1],\ [A_1\ B_1].$$

When u is a multiple of b, the number of blocks, let $w_1 = u/b$. Then a L-design with parameters $v = 4u, b, r = h/w_1, k = 8h, p = 4h, q = 2$ is given by the following blocks,

$$\underbrace{[A_{(i-1)w_1+1}\ A_{(i-1)w_1+2}\cdots A_{iw_1}\ B_{(i-1)w_1+1}\ B_{(i-1)w_1+2}\cdots B_{iw_1}}_{a\ times}$$

$$\underbrace{A_{iw_1+1}\ A_{iw_1+2}\cdots A_{(i+1)w_1}\ B_{iw_1+1}\ B_{iw_1+2}\cdots B_{(i+1)w_1}]}_{(h/w_1-a)\ times}$$

$$i = 1, 2, \cdots, b-1,$$

$$\underbrace{[A_{(b-1)w_1+1}\ A_{(b-1)w_1+2}\cdots A_{bw_1}\ B_{(b-1)w_1+1}\ B_{(b-1)w_1+2}\cdots B_{bw_1}}_{a\ times}$$

$$\underbrace{A_1\ A_2\cdots A_{w_1}\ B_1\ B_2\cdots B_{w_1}}_{(h/w_1-a)\ times}].$$

L-designs for $q \geq 4$ can be obtained by some juxtaposition of the blocks of L-designs with $q = 2$. Latin square type arrangements for each of the blocks of D can also be used which result in L-designs with $p = q$.

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