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A-Efficient Block Designs for Multiple Parallel Line Assays

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SUMMARY

A-optimality aspects of block designs for multiple parallel line assays for comparing odd number of test preparations with a single standard preparation have been studied. A general method of construction of A-optimal/efficient block designs for three major contrasts of interest, namely preparation, combined regression and parallelism contrasts have been obtained. A catalogue of 58 A-efficient block designs is also provided for comparing three test preparations with one standard preparation with $3 \le m \le 8$, $8 \le k \le 16$, $k < 4m$, $bk \le 75$ where m is the number of doses of each preparation, b the number of blocks and k is block size along with the lower bounds to their A-efficiency. A-Optimality of block designs for multiple parallel line assays that allow estimation of three contrasts of major importance but do not necessarily allow the estimability of other treatment contrasts has also been studied and a method to obtain such designs has also been developed. A catalogue of 23 A-optimal block designs for $3 \le m \le 8$, $k = 8$, $bk \le 75$ has been prepared for one standard and three test preparations.

Key words: Multiple parallel line assays, A-optimality, Estimability, Incomplete block designs for bio-assays.

1. INTRODUCTION

In many practical situations for conducting experiments on biological assays, the interest of the experimenter lies in comparing several test preparations with a single standard preparation. Consider, for example that an assay was conducted to test the three preparations of streptomycin against a standard. Two levels of doses were used for each preparation. A plate containing 64 cavities in eight rows was used for this purpose. The cavities were filled with agar and inoculated with *Bacillus subtilis*. Each cavity received a dose of streptomycin and the response was measured as the diameter of the zone of inhibition of bacterial growth. For more details on this and other examples involving more than one test preparations, one may refer to Finney (1978). In these situations, conducting separate experiment for each comparison is expensive and not practical. Multiple parallel line assays can be of help in such situations.

Several authors have studied incomplete block designs for parallel line assays involving one standard and one test preparation. A comprehensive account for the developments in this area can be found in Gupta and Mukerjee (1996). Mukerjee and Gupta (1995) initiated the work on optimality aspects of incomplete block designs for parallel line assays followed by Mukerjee (1997) with reference to the D-optimality criterion. In parallel line assays three major contrasts of importance are preparation, combined regression and parallelism. Mukerjee and Gupta (1995) presented A-optimal/ efficient designs for the estimation of these three contrasts in the context of symmetric parallel line assays. It has been observed that often a non-equireplicate design has higher A-efficiency in comparison to a comparable equireplicate design. These designs require that the block sizes should be integral multiple of four and are not always connected and, therefore, do not always ensure estimability of all contrasts among those effects. Chai *et al.* (2001) have considered the problem of obtaining A-optimal block designs for the estimation of the two major contrasts namely, preparation and combined regression in the context of both symmetric and asymmetric parallel line assays. Srivastava *et al.* (2007) have obtained A-efficient designs for estimation of all the three contrasts of major importance.

The literature on block designs for multiple parallel line assays is rather scanty. Das (1985) has given a method of constructing block designs for multiple parallel line assays using affine resolvable block designs and C-designs. Limitation of this method is that the designs obtained are very large even for small parameters. Further, the optimality aspects of these designs have not been discussed.

Keeping this in view, in this communication A-optimality of block designs for parallel line assays for the situations in which the experimenter is interested in comparing several test preparations with a single standard preparation has been studied in Section 3. The study is restricted to odd number of test preparations and one standard preparation. A method of generation of A-optimal/efficient block designs for symmetric multiple parallel line assays for estimation of all the three contrasts of interest, namely preparation, combined regression and parallelism has been given in Section 4. As a special case, we present a catalogue of incomplete block designs for multiple parallel line assays for one standard and three test preparations with $3 \le m \le 8$, $8 \le k \le 16$, $k < 4m$, $bk \le 75$ where m is the number of doses of each preparation, b the number of blocks and k is block size along with the lower bounds to their A-efficiency in Table 1 (Appendix 3).

In multiple parallel line assays, the main interest is in estimating only the three contrasts and the experimenter may not be interested in other treatment contrasts. For such situations one might think of designs that ensure estimability of these three contrasts but do not guarantee the estimability of other contrasts. Keeping this in view, A- optimality of block designs for multiple parallel line assays that ensure the estimability of the three contrasts in question and these designs are necessarily disconnected otherwise has been investigated. A general method of construction of disconnected block designs for multiple parallel line assays that ensure the estimability of the three contrasts of interest is given in Section 5. A catalogue of the designs obtainable from this method of construction for $3 \le m \le 8$, $k = 8$, $bk \le 75$ is given in Table 2 in Appendix 3. We begin with some preliminaries in Section 2.

2. PRELIMINARIES

Consider conducting bioassay with one standard preparation and odd number of test preparations, $c \ge 1$ using an incomplete block design. Let s and $t^{(q)}$ denote the doses of standard and test preparations respectively, q = 1, 2, ..., c. Let the doses of standard preparations be denoted by s_i, i = 1,... m and $t_i^{(q)}$ represents the i^{th} dose of q^{th} test preparation; i = 1, 2, ..., m; q = 1, 2, ..., c. These doses are equispaced on the logarithmic scale, the common ratio being same for all the preparations. Let $\boldsymbol{\tau} = (\tau_1, \tau_2, \ldots, \tau_m, \tau_{m+1}, \ldots, \tau_v)'$ be the vector of dose effects, $v = (c+1)m$. Then the three major contrasts namely preparation, combined regression and parallelism in the normalized form are given respectively as follows:

$$\mathbf{U}_1 = \frac{1}{\sqrt{2m}}\left(\mathbf{1}_c \otimes \mathbf{1}'_m \quad : \quad -\mathbf{I}_c \otimes \mathbf{1}'_m\right)$$

$$\mathbf{U}_2 = \sqrt{\frac{12}{m(m^2-1)(c+1)}}\left(\mathbf{1}'_{c+1} \otimes \mathbf{w}'\right)$$

$$\mathbf{U}_3 = \sqrt{\frac{6}{m(m^2-1)}}\left(\mathbf{1}_c \otimes \mathbf{w}' \quad : \quad -\mathbf{I}_c \otimes \mathbf{w}'\right)$$

where $\mathbf{w} = (1, 2, \ldots, m)' - \frac{1}{2}(m+1)\mathbf{1}'_m$.

3. OPTIMALITY ASPECTS

Consider that a symmetric parallel line assay involving m (≥2) doses each of standard preparation and c test preparations for c odd is run using an incomplete block design. For given v = (c + 1) m, the number of blocks and k the block size, we define $\mathbf{D} \equiv \mathbf{D}(v, b, k)$, the class of all block designs involving v doses, b blocks each of size k. For any design $d \in \mathbf{D}$, let r_{s_i} and $r_{t_i^{(q)}}$ be the replication of dose of i^{th} standard preparation and q^{th} test preparation, respectively, $i = 1, 2, \ldots, m$; q = 1, 2, ..., c. Let $\mathbf{R}_d = \text{diag}(r_{s_1}, r_{s_2}, \ldots, r_{s_m}, r_{t_1(1)}, \ldots, r_{t_m(1)}, r_{t_1^{(2)}}, \ldots, r_{t_m^{(2)}}, \ldots, r_{t_1^{(c)}}, \ldots, r_{t_m^{(c)}})$, $\mathbf{N}_d$ be the v × b incidence matrix of d and $\mathbf{C}_d = \mathbf{R}_d - k_d^{-1}\mathbf{N}_d\mathbf{N}'_d$. A fixed effects additive model is assumed for the data collected through d with the assumption that the errors are independent with zero mean and common variance σ^2. Every treatment contrast is estimable if and only if Rank ($\mathbf{C}_d$) = v – 1 and a design that allows estimation of all treatment contrasts is called a connected design. Define $\mathbf{D}_1$ to be the sub class of $\mathbf{D}$ in which $\mathbf{U}\boldsymbol{\tau}$ is estimable and $\mathbf{D}_2$ be the class of all connected block designs. Clearly, $\mathbf{D}_2 \subset \mathbf{D}_1$. Let $\mathbf{V}_d$ be the variance-covariance matrix of $\mathbf{U}\hat{\boldsymbol{\tau}}$, where $\mathbf{U}\hat{\boldsymbol{\tau}}$ is the best linear unbiased estimator of $\mathbf{U}\tau$ under d and $\mathbf{U}$ is (2c + 1) × v matrix with rows as $\mathbf{U}_1$, $\mathbf{U}_2$ and $\mathbf{U}_3$. An A-optimal design for $\mathbf{U}\tau$ in $\mathbf{D}$ is the one, which belongs to $\mathbf{D_2}$ and minimizes the trace ($\mathbf{V}_d$) over $\mathbf{D_1}$, where trace (.) denotes trace of a matrix. Here, we consider only those designs that fulfill this criterion.

Following Gupta and Mukerjee (1996), it can be seen that $\sigma^{-2}\mathbf{V}_d - \mathbf{U}\mathbf{R}_d^{-1}\mathbf{U}'$ is non-negative definite for any d ∈ $\mathbf{D_1}$. Hence, for each d ∈ $\mathbf{D_1}$

$$\sigma^{-2}\,\mathrm{trace}(\mathbf{V}_d) \ge \mathrm{trace}\left(\mathbf{U}\mathbf{R}_d^{-1}\mathbf{U}'\right)$$

$$= \sum_{i=1}^{m} \alpha_{s_i} / r_{s_i} + \sum_{q=1}^{c}\sum_{i=1}^{m} \alpha_{t_i}^{q} / r_{t_i}^{q} \quad \text{where for } 1 \le i \le m \quad (3.1)$$

$$\alpha_{s_i} = \frac{c}{2m} + \frac{6}{m\left(m^2-1\right)}\left(\frac{2}{c+1}+c\right)\left\{i - \frac{m+1}{2}\right\}^2,$$

$$\alpha_{t_i^{(q)}} = \frac{1}{2m} + \frac{6}{m\left(m^2-1\right)}\left(\frac{2}{c+1}+1\right)\left\{i - \frac{m+1}{2}\right\}^2,$$

for q = 1, 2, ..., c. (3.2)

Suppose now that $d_0 \in \mathbf{D}_2$ such that

$$\sigma^{-2}\mathbf{V}_{d_0} = \mathbf{U}\mathbf{R}_{d_0}^{-1}\mathbf{U}' \quad (3.3)$$

A design d_0 is A-optimal over $\mathbf{D}$ if d_0 minimizes the right hand side of (3.3). Appealing to Lemma 3.1 of Gupta and Mukerjee (1996), (3.3) holds if and only if

$$\mathbf{U}\mathbf{R}_{d_0}^{-1}\mathbf{N}_{d_0} = \mathbf{0} \quad (3.4)$$

where $\mathbf{N}_{d_0}$ is v × b incidence matrix of design d_0.

If all the three contrasts are considered, (3.4) is generally not achievable via the method of construction of Chai *et al*. (2001), a lower bound to the A-efficiency may be obtained and using this lower bound, designs with high A-efficiencies for all the three contrasts can be obtained. In the sequel, we attempt to achieve this.

4. METHOD OF CONSTRUCTION

In this paper we restrict to the case of conducting parallel line assay with one standard and c test preparations, where c is odd. The method of construction is in accordance with the method proposed by Chai *et al.* (2001). For completeness we describe below the steps to be taken to arrive at an A-optimal design over $\mathbf{D}$.

(i) Let $$\gamma = \min\left\{\sum_{i=1}^{m} \alpha_{s_i} / p_i + \sum_{q=1}^{c}\sum_{i=1}^{m} \alpha_{t_i^{(q)}} / p_i\right\} \quad (4.1)$$

the minimum being taken with respect to $\mathbf{z} = (p_1, p_2 ..., p_m)'$ where p_i's are positive integers satisfying $(c+1)\sum_{i=1}^{m} p_i = bk$.

Let $\mathbf{z}^* = (p_1^*, p_2^*, ..., p_m^*)'$ be a choice of $\mathbf{z}$ where this minimum is attained. Then from (3.1), $\sigma^{-2}\,\mathrm{trace}(\mathbf{V}_d) \ge \gamma$.

(ii) Construct a block design $d^* \in \mathbf{D_2}$ with v = (c + 1) m, b blocks of size k each, such that for 1 ≤ i ≤ (c +1) m the i^{th} dose of the preparations is replicated p_i^* times in d^*. Further, $\mathbf{N}_{d^*}$ satisfies (3.4). Then $\sigma^{-2}\mathrm{trace}(\mathbf{V}_d) \ge \gamma = \sigma^{-2}\mathrm{trace}\left(\mathbf{V}_{d^*}\right)$. Hence, d^* is an A-optimal block design in $\mathbf{D}$. As mentioned earlier, if (3.4) is not satisfied we end up in achieving lower bound to A-efficiency. For completeness, we give below various steps for the construction of the designs on the lines similar to that of Chai *et al*. (2001).

Step 1: Let $G_i = \left\{i, m+i, ..., \left(\frac{c-1}{2}\right)m+i, \left(\frac{c+3}{2}\right)m+1-i, ..., (c+1)m+1-i\right\}$, $1 \le i \le m$. Then, G_i's provide disjoint partition of $\{1, 2, ..., v\}$ with $v = (c+1)m$.

Step 2 : Find γ as in (i).

Step 3 : Construct a connected block design d_1 with b blocks each of size k /(c + 1) involving m treatments, say $\theta_1, \theta_2, ..., \theta_m$ such that θ_i is replicated p_i^* times in d_1, $1 \le i \le m$.

Step 4 : Obtain a design d^* from d_1 by replacing the treatment θ_i in d_1 by the (c + 1) treatments in the set G_i.

To be clearer, consider the following example.

Designs obtained through the method described above sometimes yield repeated blocks. We represent repeated blocks by a number in parenthesis just after the (repeated) contents.

Example 4.1: Let $c = 3,\ m = 3,\ k = 8$ and $b = 4$. The disjoint partitions are $G_1 = \{1,\ 4,\ 9,\ 12\} = \theta_1$, $G_2 = \{2, 5, 8, 11\} = \theta_2$ and $G_3 = \{3,\ 6,\ 7,\ 10\} = \theta_3$. Here $p_1^* = p_4^* = p_9^* = p_{12}^* = 3,\ p_2^* = p_5^* = p_8^* = p_{11}^* = 2$ and $p_3^* = p_6^* = p_7^* = p_{10}^* = 3$. Let d_1 be the design with four blocks as (θ_1,θ_2), (θ_1,θ_3) repeated two times, (θ_2,θ_3). Then the design d_1 is given by {1, 2, 4, 5, 8, 9, 11, 12}; {1, 3, 4, 6, 7, 9, 10, 12}(2); {2, 3, 5, 6, 7, 8, 10, 11}.

5. DISCONNECTED BLOCK DESIGNS FOR MULTIPLE PARALLEL LINE ASSAYS

Srivastava *et al*. (2007) in the context of parallel line assays have proposed disconnected block designs that are A-optimal for the estimation of major contrasts of interest but do not guarantee the estimability of other treatment contrasts. In this section, we adopt similar approach to obtain A-optimal block designs for multiple parallel line assays. A general method of construction of such designs with odd number of test preparations is given below.

Step 1: As in Section 4, let

$$G_i = \left\{i, m+i, ..., \left(\frac{c-1}{2}\right)m+i, \left(\frac{c+3}{2}\right)m+1-i, ..., (c+1)m+1-i\right\},\ 1 \le i \le m$$

provide a disjoint partition of {1, 2, ..., V}, $v = (c+1)m$. Let the sub-set G_i denote a treatment θ_i, i = 1, 2, ..., m.

Step 2: Find $\mathbf{z}^* = (p_1^*,\ p_2^*,\ ...,\ p_m^*)'$ and γ as in (4.1).

Step 3: For $v = (c+1)m,\ m = 2\mu$, μ is a positive integer, choose only those designs for which $p_u^{**} = p_{qm+u}^* = p_{(q+1)m-u+1}^*$, $1 \le u \le \mu, 0 \le q \le c$. For $v = (c+1)m$, $m = 2\mu+1$, choose only those designs for which $p_u^{**} = p_{qm+u}^* = p_{(q+1)m-u+1}^*$, for $1 \le u \le \mu$, $0 \le q \le c$ and $p_{\mu+1}^{**} = p^*_{\frac{(2q+1)m+1}{2}} = 2t$, t is positive integer and $0 \le q \le c$.

Step 4: Construct a block design d_1 with b blocks each of size 2 involving m treatments, $\theta_1,\ \theta_2, ..., \theta_m$ such that θ_j appears with θ_{m-j+1} in p_j^* blocks, $1 \le j \le m$. For $m = 2\mu+1$, the block containing $\theta_{\frac{m+1}{2}}$ twice is repeated t times.

Step 5: Obtain a design d^* from d_1 by replacing the treatment θ_j in d_1 by (c + 1) treatments in G_j, $1 \le j \le m$.

It may be noted that for $v = (c+1)m$, m = 2μ, the total number of blocks in d_1 is $b = \sum_{u=1}^{\mu} p_u^{**}$ while for $v = (c+1)m$, $m = 2\mu+1$, the total number of blocks in d_1 is $b = \sum_{u=1}^{\mu} p_u^{**} + t$.

We present below designs obtainable through above method of construction in terms of the structure of incidence matrix, separately for both even and odd number of doses. This representation is helpful in proving the A-optimality of these designs that ensure estimability of the three major contrasts of importance.

5.1 Block Designs with Even Number of Doses

For even number of doses, block designs with $v = (c+1)m = 2(c+1)\mu$ and $k = 2(c+1)$ can easily be constructed after obtaining p_u^{**}, $1 \le u \le \mu$ in Step 3. For some integer n, let $\mathbf{I}_n^*$ be an $n \times n$ matrix given by

$$\mathbf{I}_n^* = \begin{bmatrix} 0 & ... & 0 & 1 \\ 0 & ... & 1 & 0 \\ ... & ... & ... & ... \\ 1 & ... & 0 & 0 \end{bmatrix}.$$

Then the v × b incidence matrix of the design is given by

$$\mathbf{N} = \mathbf{1}_{(c+1)} \otimes \begin{bmatrix} \mathbf{M} \\ \mathbf{M}^* \end{bmatrix} \tag{5.1}$$

where **M** is the μ × b matrix given by

$$\mathbf{M} = \bigoplus_{u=1}^{\mu} \mathbf{1}'_{p_u^{**}}, \tag{5.2}$$

$\bigoplus_{u=1}^{\mu}$ denoting the direct sum of matrices, $\mathbf{M}^*$ is μ × b matrix obtained by taking the mirror image of **M**, i.e., $\mathbf{M}^* = \mathbf{I}^*_{\mu}\mathbf{M}$, ⊗ denotes the Kronecker product of matrices and $\mathbf{1}_t$ is a t × 1 vector of ones. We illustrate this with the following example.

Example 5.1: Let c = 3, m = 6, b = 6 and k = 8. For this design $p_1^{**} = 3$, $p_2^{**} = 2$, $p_3^{**} = 1$ and **M** and $\mathbf{M}^*$ are

$$\mathbf{M} = \begin{bmatrix} 1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix},$$

$$\mathbf{M}^* = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & 1 & 0 \\ 1 & 1 & 1 & 0 & 0 & 0 \end{bmatrix}.$$

The block contents of the design are given by {1,6,7,12,13,18,19,24}(3); {2,5,8,11,14,17,20,23}(2); {3,4,9,10,15,16,21,22}. This design is A-optimal for estimating three contrasts of importance. The corresponding connected block design with the same parameters (given at S. No. 32 of Table 1 Appendix 3) has efficiency 0.9008. Further, the efficiency of parallelism contrast is only 0.7591.

5.2 Designs with Odd Number of Doses

For odd number of doses, the block designs with $v = (c+1)m$, $m = 2\mu + 1$ and $k = 2(c+1)$ can easily be constructed after obtaining p_u^{**}, $1 \le u \le \mu + 1$ in step 3. The $v \times b$ incidence matrix is given by

$$\mathbf{N} = \mathbf{1}_{(c+1)} \otimes \begin{bmatrix} \mathbf{M}_{\mu \times b^*} & \mathbf{0}_{\mu \times t} \\ \mathbf{0}'_{b^*} & 2\mathbf{1}'_t \\ \mathbf{M}^*_{\mu \times b^*} & \mathbf{0}_{\mu \times t} \end{bmatrix} \tag{5.3}$$

where $b^* = b - t$, $\mathbf{M} = \bigoplus_{u=1}^{\mu} + \mathbf{1}'_{p_u^{**}}$ and $\mathbf{M}^*$ is as defined earlier.

Example 5.2: Let c = 3, m = 5, b = 6 and k = 8. For this design $p_1^{**} = 3$, $p_2^{**} = 2$, $p_3^{**} = 2$. Here the matrix **M** is given by

$$\mathbf{M} = \begin{bmatrix} 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 \end{bmatrix},$$

and the design is given by {1, 5, 6, 10, 11, 15, 16, 20}(3); {2, 4, 7, 9, 12, 14, 17, 19}(2); {3, 3, 8, 8, 13, 13, 18, 18}. The corresponding connected design (at S. No. 18 of Table 1) has efficiency 0.9519, whereas the design obtained in this example is A-optimal for estimating the three contrasts of interest.

It may be observed easily that the designs constructed in this section are necessarily disconnected. However, these designs ensure the estimability of all the three major contrasts of importance. We, thus, have the following theorem:

Theorem 5.1. The design d^* obtained by following Steps 1-5 in the method described earlier is disconnected but the three major contrasts of importance are estimable through d^*.

Proof. The proof is given in Appendix 1.

From the above methods of construction and the structure of **N** (both for even and odd m) one can easily show that $\mathbf{U}\mathbf{R}^{-1}\mathbf{N} = \mathbf{0}$. Further, the designs so obtained satisfy (4.1) and thus (3.4). Therefore, the design d^* is A-optimal. Thus, we have

Theorem 5.2. The design d^* obtained by following Steps 1-5 in the methods described earlier is A-optimal for estimating all the three contrasts of major importance.

Proof. The proof is given in Appendix 2.

6. DISCUSSIONS AND TABLES OF DESIGNS

In Table 1 (Appendix 3), A-efficient block designs for multiple symmetric parallel line assays for three test reparations and one standard preparation are presented. Complete solution of the designs is given in the column of block contents. Repeated blocks are shown by a number in parentheses just after the (repeated) block. Similarly, "+dx" indicates that the blocks of design number "x" are to be added to the other block(s) shown in the same row.

For any single treatment contrast $\mathbf{q}'\boldsymbol{\tau}$, estimable in a block design, it is known that $\text{var}(\mathbf{q}'\hat{\boldsymbol{\tau}}) = \sigma^2 \mathbf{q}'\mathbf{C}^-\mathbf{q}$, where $\mathbf{C}^-$ is a generalized inverse of **C**, the information matrix of the block design. From Lemma 3.1 of Gupta and Mukerjee (1996), $\text{var}(\mathbf{q}'\hat{\boldsymbol{\tau}}) \geq \sigma^2 \mathbf{q}'\mathbf{R}^{-1}\mathbf{q}$. Now, let V_1 denote theoretical lower bound to sum of variances of best linear unbiased estimators (BLUEs) of the three contrasts and V_2, the sum of variances of BLUEs of these contrasts under our designs. A lower bound to A-efficiency is, therefore, given by $e = V_1/V_2$. Again let V_3 denote theoretical lower bound of variance of BLUE of the parallelism contrast and V_4 the variance of BLUE of parallelism contrast under our designs. A lower bound to efficiency of the parallelism contrast is given by $e_1 = V_3/V_4$. The values of e and e_1 are given in the Table 1 (Appendix 3).

We have catalogued 58 designs along-with their A-efficiencies. SAS programs are extensively used for finding A-optimal incomplete block designs for bioassays and the program for obtaining optimum p_i^{**}'s is available with the authors.

The disconnected block designs that ensure the estimation of three contrasts of interest obtained through the above method of construction with c = 3, $3 \leq m \leq 8$, $k = 8$, $bk \leq 75$ are presented in Table 2 (Appendix 3). These designs are A-optimal for estimation of the three contrasts of interest.

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APPENDIX 1

Proof of Theorem 5.1

(a) m (= 2μ) even

The concurrence matrix $\mathbf{NN}'$ for the design is

$$\mathbf{NN}' = \mathbf{J}_{c+1} \otimes \mathbf{R}_m \,.$$

where $\mathbf{R}_m = \begin{bmatrix} \mathbf{R}_\mu & \mathbf{R}_\mu^* \\ \bar{\mathbf{R}}_\mu^* & \bar{\mathbf{R}}_\mu \end{bmatrix}$, $\mathbf{R}_\mu$= diag $(p_1^{**}, p_2^{**}, ..., p_\mu^{**})$, $\bar{\mathbf{R}}_\mu$ = diag$(p_\mu^{**}, p_{\mu-1}^{**}, ..., p_1^{**})$, $\mathbf{R}_\mu^* = \mathbf{R}_\mu \mathbf{I}_\mu^*$ and $\bar{\mathbf{R}}_\mu^* = \mathbf{I}_\mu^* \mathbf{R}_\mu$. $\mathbf{R} = \mathbf{I}_{c+1} \otimes \mathbf{R}_d$ where $\mathbf{R}_d = \text{diag}\left(\mathbf{R}_\mu \quad \bar{\mathbf{R}}_\mu\right)$. The **C** matrix is given by

$$\mathbf{C} = \frac{1}{2(c+1)}\left[\mathbf{I}_{c+1} \otimes (\mathbf{R}_c + \mathbf{R}_m) - \mathbf{J}_{c+1} \otimes \mathbf{R}_m\right]$$

where $\mathbf{R}_c = \begin{bmatrix} (2c+1)\mathbf{R}_\mu & -\mathbf{R}_\mu^* \\ -\bar{\mathbf{R}}_\mu^* & (2c+1)\bar{\mathbf{R}}_\mu \end{bmatrix}$.

Rank $(\mathbf{C}) = (c+1)m - (m/2)$ and thus the design is disconnected for m > 2. A linear function of treatment effects, $\mathbf{q}'\boldsymbol{\tau}$ is estimable if and only if $\mathbf{q}'\mathbf{C}^-\mathbf{C} = \mathbf{q}'$, where $\mathbf{C}^-$ is a generalized inverse of **C**. In our case $\mathbf{C}^-$ is given by

$$\mathbf{C}^- = \begin{bmatrix} \mathbf{R}_0^c & \mathbf{1}_c' \otimes \mathbf{R}_0^{m\prime} \\ \mathbf{1}_c \otimes \mathbf{R}_0^m & \mathbf{I}_c \otimes \left(\mathbf{R}^c - \mathbf{R}^m\right) + \mathbf{J}_c \otimes \mathbf{R}^m \end{bmatrix}$$

where $\mathbf{R}^c = \begin{bmatrix} 2\mathbf{R}_\mu^{-1} & \bar{\mathbf{R}}_\mu^{*-1} \\ \mathbf{R}_\mu^{*-1} & 2\bar{\mathbf{R}}_\mu^{-1} \end{bmatrix}$, $\mathbf{R}^m = \begin{bmatrix} \mathbf{R}_\mu^{-1} & \bar{\mathbf{R}}_\mu^{*-1} \\ \mathbf{R}_\mu^{*-1} & \bar{\mathbf{R}}_\mu^{-1} \end{bmatrix}$

$$\mathbf{R}_0^c = \begin{bmatrix} \mathbf{0} & \mathbf{0} \\ \mathbf{0} & 2\bar{\mathbf{R}}_\mu^{-1} \end{bmatrix} \text{ and } \mathbf{R}_0^m = \begin{bmatrix} \mathbf{0} & \bar{\mathbf{R}}_\mu^{*-1} \\ \mathbf{0} & \bar{\mathbf{R}}_\mu^{-1} \end{bmatrix}.$$

Then
$$\mathbf{C}^-\mathbf{C} = \begin{bmatrix} \mathbf{0}_{\mu\times\mu} & \mathbf{0}_{\mu\times\mu} & \mathbf{0}_{\mu\times 2c\mu} \\ -\mathbf{I}_\mu^* & \mathbf{I}_\mu & \mathbf{0}_{\mu\times 2c\mu} \\ -\mathbf{1}_c \otimes \begin{bmatrix} \mathbf{I}_\mu \\ \mathbf{I}_\mu^* \end{bmatrix} & \mathbf{0}_{2c\mu\times\mu} & \mathbf{I}_{2c} \otimes \mathbf{I}_\mu \end{bmatrix}.$$

Consider now the matrix **U** of normalized treatment contrasts as given in (3.1). We partition **w** as $\mathbf{w} = \left(\mathbf{w}_1' \quad \mathbf{w}_2'\right)'$ such that $\mathbf{w}_1(\mathbf{w}_2)$ contains first (last) μ elements of **w**. As $\mathbf{w}_1' = -\mathbf{w}_2'\mathbf{I}_\mu^*$, it can easily be seen that $\mathbf{UC}^-\mathbf{C} = \mathbf{U}$. Thus, the contrasts $\mathbf{U}\boldsymbol{\tau}$ are estimable using the design **d***.

(b) m (= 2μ + 1) odd

The concurrence matrix $\mathbf{NN}'$ is given by

$$\mathbf{NN}' = \mathbf{J}_{c+1} \otimes \mathbf{R}_m$$

where $\mathbf{R}_m = \begin{bmatrix} \mathbf{R}_\mu & \mathbf{0} & \mathbf{R}_\mu^* \\ \mathbf{0}' & 2p_{\mu+1}^{**} & \mathbf{0}' \\ \bar{\mathbf{R}}_\mu^* & \mathbf{0} & \bar{\mathbf{R}}_\mu \end{bmatrix}$.

$\mathbf{R} = \mathbf{I}_{c+1} \otimes \mathbf{R}_d$ where $\mathbf{R}_d = \text{diag}\left(\mathbf{R}_\mu \quad p_{\mu+1}^{**} \quad \bar{\mathbf{R}}_\mu\right)$
The **C** matrix is given by

$$\mathbf{C} = \frac{1}{2(c+1)}\left[\mathbf{I}_{c+1} \otimes (\mathbf{R}_c + \mathbf{R}_m) - \mathbf{J}_{c+1} \otimes \mathbf{R}_m\right]$$

where $\mathbf{R}_c = \begin{bmatrix} (2c+1)\mathbf{R}_\mu & \mathbf{0} & -\mathbf{R}_\mu^* \\ \mathbf{0}' & 2p_{\mu+1}^{**} & \mathbf{0}' \\ -\bar{\mathbf{R}}_\mu^* & \mathbf{0} & (2c+1)\bar{\mathbf{R}}_\mu \end{bmatrix}$.

Rank **(C)** $= (c+1)m - \dfrac{(m+1)}{2}$ and thus the design is disconnected for $m \geq 3$.

$$\mathbf{C}^- = \begin{bmatrix} \mathbf{R}_0^c & \mathbf{1}_c' \otimes \mathbf{R}_0^{m\prime} \\ \mathbf{1}_c \otimes \mathbf{R}_0^m & \mathbf{I}_c \otimes \left(\mathbf{R}^c - \mathbf{R}^m\right) + \mathbf{J}_c \otimes \mathbf{R}^m \end{bmatrix}$$

where $\mathbf{R}^c = \begin{bmatrix} 2\mathbf{R}_\mu^{-1} & \mathbf{0} & \bar{\mathbf{R}}_\mu^{*-1} \\ \mathbf{0}' & \dfrac{2}{p_{\mu+1}^{**}} & \mathbf{0}' \\ \mathbf{R}_\mu^{*-1} & 0 & 2\bar{\mathbf{R}}_\mu^{-1} \end{bmatrix}$,

$$\mathbf{R}^{m} = \begin{bmatrix} \mathbf{R}_{\mu}^{-1} & \mathbf{0} & \bar{\mathbf{R}}_{\mu}^{*-1} \\ \mathbf{0}' & \mathbf{0} & \mathbf{0}' \\ \mathbf{R}_{\mu}^{*-1} & \mathbf{0} & \bar{\mathbf{R}}_{\mu}^{-1} \end{bmatrix}, \quad \mathbf{R}_0^{c} = \begin{bmatrix} \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0}' & \mathbf{0} & \mathbf{0}' \\ \mathbf{0} & \mathbf{0} & 2\bar{\mathbf{R}}_{\mu}^{-1} \end{bmatrix}$$

and $\mathbf{R}_0^{m} = \begin{bmatrix} \mathbf{0} & \mathbf{0} & \bar{\mathbf{R}}_{\mu}^{*-1} \\ \mathbf{0}' & \mathbf{0} & \mathbf{0}' \\ \mathbf{0} & \mathbf{0} & \bar{\mathbf{R}}_{\mu}^{-1} \end{bmatrix}$.

Then

$$\mathbf{C}^{-}\mathbf{C} = \begin{bmatrix} \mathbf{0}_{(\mu+1)\times(\mu+1)} & \mathbf{0}_{(\mu+1)\times\mu} & \mathbf{0}_{(\mu+1)\times c(2\mu+1)} \\ \left[-\mathbf{I}_{\mu}^{*} \quad \mathbf{0}_{\mu\times1}\right] & \mathbf{I}_{\mu} & \mathbf{0}_{\mu\times c(2\mu+1)} \\ \mathbf{X}_1 & \mathbf{0}_{c(2\mu+1)\times\mu} & \mathbf{X}_2 \end{bmatrix}$$

where $\mathbf{X}_1 = \mathbf{1}_c \otimes \begin{bmatrix} -\mathbf{I}_{\mu} & \mathbf{0}_{\mu\times1} \\ \mathbf{0}'_{1\times\mu} & -1 \\ -\mathbf{I}_{\mu}^{*} & \mathbf{0}_{\mu\times1} \end{bmatrix}$ and

$$\mathbf{X}_2 = \mathbf{I}_c \otimes \begin{bmatrix} \mathbf{I}_{\mu} & \mathbf{0}_{\mu\times1} & \mathbf{0}_{\mu\times\mu} \\ \mathbf{0}'_{1\times\mu} & 1 & \mathbf{0}'_{1\times\mu} \\ \mathbf{0}_{\mu\times\mu} & \mathbf{0}_{\mu\times1} & \mathbf{I}_{\mu} \end{bmatrix}.$$

The proof of estimability follows on the lines of proof for even number of doses and noting that in this case $\mathbf{w} = \left(\mathbf{w}_1' \quad 0 \quad \mathbf{w}_2'\right)'$.

APPENDIX 2

Proof of Theorem 5.2

(a) m (= 2μ) even

As per the Method 5.1 we have

$$\mathbf{N} = \mathbf{1}_{(c+1)} \otimes \begin{bmatrix} \mathbf{M} \\ \mathbf{M}^{*} \end{bmatrix}.$$

Therefore, $\mathbf{R}^{-1}\mathbf{N} = \mathbf{1}_{(c+1)} \otimes \begin{bmatrix} \mathbf{R}_{\mu}^{-1}\mathbf{M} \\ \bar{\mathbf{R}}_{\mu}^{-1}\mathbf{M}^{*} \end{bmatrix}$.

We have $\mathbf{U}\mathbf{R}^{-1}\mathbf{N} = \begin{bmatrix} \mathbf{U}_1\mathbf{R}^{-1}\mathbf{N} \\ \mathbf{U}_2\mathbf{R}^{-1}\mathbf{N} \\ \mathbf{U}_3\mathbf{R}^{-1}\mathbf{N} \end{bmatrix}$.

Writing

$$\mathbf{U}_1 = \frac{1}{\sqrt{2m}}\left[\mathbf{1}_c \otimes \left(\mathbf{1}_{\mu}' \quad \mathbf{1}_{\mu}'\right) \quad : \quad \mathbf{I}_c \otimes \left(-\mathbf{1}_{\mu}' \quad -\mathbf{1}_{\mu}'\right)\right],$$

we have $\mathbf{U}_1\mathbf{R}^{-1}\mathbf{N} = \mathbf{0}'$.

We partition $\mathbf{w}$ as $\mathbf{w} = \left(\mathbf{w}_1' \quad \mathbf{w}_2'\right)'$ such that $\mathbf{w}_1(\mathbf{w}_2)$ contains first (last) μ elements of $\mathbf{w}$. It is easy to see that $\mathbf{w}_1' = -\mathbf{w}_2'\mathbf{I}_{\mu}^{*}$. As a consequence

$$\mathbf{U}_2 = \sqrt{\frac{12}{m(m^2-1)(c+1)}}\left(\mathbf{1}_{c+1}' \otimes \mathbf{w}'\right) \text{ and, therefore,}$$

$$\mathbf{U}_2\mathrm{R}^{-1}\mathbf{N} = \sqrt{\frac{12(c+1)}{m(m^2-1)}}\left[\mathbf{w}_1'\mathbf{R}_{\mu}^{-1}\mathbf{M} + \mathbf{w}_2'\bar{\mathbf{R}}_{\mu}^{-1}\mathbf{M}^{*}\right]$$

$$= \sqrt{\frac{12(c+1)}{m(m^2-1)}}\left(-\mathbf{w}_2'\mathbf{I}_{\mu}^{*}\mathbf{R}_{\mu}^{-1}\mathbf{M} + \mathbf{w}_2'\bar{\mathbf{R}}_{\mu}^{-1}\mathbf{I}_{\mu}^{*}\mathbf{M}\right) = \mathbf{0}'$$

since $\mathbf{I}_{\mu}^{*}\mathbf{R}_{\mu}^{-1} = \bar{\mathbf{R}}_{\mu}^{-1}\mathbf{I}_{\mu}^{*}$.

Again, $\mathbf{U}_3 = \sqrt{\frac{6}{m(m^2-1)}}\left(\mathbf{1}_c \otimes \mathbf{w}' \quad : \quad -\mathbf{I}_c \otimes \mathbf{w}'\right)$ and we have $\mathbf{U}_3\mathbf{R}^{-1}\mathbf{N} = \mathbf{0}'$.

(b) *m* (= 2μ + 1) odd

As per Method 5.1, we have

$$\mathbf{N} = \mathbf{1}_{c+1} \otimes \begin{bmatrix} \mathbf{M} & \mathbf{0} \\ \mathbf{0}' & p_{\mu+1}^{**} \\ \mathbf{M}^{*} & \mathbf{0} \end{bmatrix}.$$

Therefore, $\mathbf{R}^{-1}\mathbf{N} = \mathbf{1}_{c+1} \otimes \begin{bmatrix} \mathbf{R}_{\mu}^{-1}\mathbf{M} & \mathbf{0} \\ \mathbf{0}' & 1 \\ \bar{\mathbf{R}}_{\mu}^{-1}\mathbf{M}^{*} & \mathbf{0} \end{bmatrix}$.

Writing

$$\mathbf{U}_1 = \frac{1}{\sqrt{2m}}\left[\mathbf{1}_c \otimes \left(\mathbf{1}_{\mu}' \quad 1 \quad \mathbf{1}_{\mu}'\right) : \mathbf{I}_c \otimes \left(-\mathbf{1}_{\mu}' \quad -1 \quad -\mathbf{1}_{\mu}'\right)\right]$$

we have $\mathbf{U}_1\mathbf{R}^{-1}\mathbf{N} = \mathbf{0}'$.

We partition $\mathbf{w}$ as $\mathbf{w} = \left(\mathbf{w}_1' \quad 0 \quad \mathbf{w}_2'\right)'$ such that $\mathbf{w}_1(\mathbf{w}_2)$ contains first (last) μ elements of $\mathbf{w}$. It is easy to see that $\mathbf{w}_1 = -\mathbf{w}_2\mathbf{I}_\mu^*$.

As a consequence

$$\mathbf{U}_2 = \sqrt{\frac{12}{m(m^2-1)(c+1)}}\left(\mathbf{1}_{c+1}' \otimes \mathbf{w}'\right)$$ and, therefore,

$$\mathbf{U}_2\mathbf{R}^{-1}\mathbf{N} = \sqrt{\frac{12(c+1)}{m(m^2-1)}}\left[\left(-\mathbf{w}_2'\mathbf{I}_\mu^*\mathbf{R}_\mu^{-1}\mathbf{M} + \mathbf{w}_2'\bar{\mathbf{R}}_\mu^{-1}\mathbf{I}_\mu^*\mathbf{M}\right) \quad 0\right] = \mathbf{0}'$$

since $\mathbf{I}_\mu^*\mathbf{R}_\mu^{-1} = \bar{\mathbf{R}}_\mu^{-1}\mathbf{I}_\mu^*$.

Again, $\mathbf{U}_3 = \sqrt{\frac{6}{m(m^2-1)}}\left(\mathbf{1}_c \otimes \mathbf{w}' \;:\; -\mathbf{I}_c \otimes \mathbf{w}'\right)$ and we have $\mathbf{U}_3\mathbf{R}^{-1}\mathbf{N} = \mathbf{0}'$. As the designs constructed satisfy (4.1) and (3.5) both for even and odd number of doses, they are A-optimal for estimating the three contrasts of major importance.

APPENDIX 3

Table 1. A-efficient block designs (connected) with c = 3, 3 ≤ m ≤ 8, 8 ≤ k ≤ 16, k < 4m, bk ≤ 75

No.	*b*	p_u^{**}	Block contents	e_1	*e*
m = 3, *k* = 8					
1.	2	2, 1, 1	{1, 2, 4, 5, 8, 9, 11, 12}; {1, 3, 4, 6, 7, 9, 10, 12}	0.9000	0.9565
2.	3	2, 2, 2	D1 + {2, 3, 5, 6, 7, 8, 10, 11}	0.9000	0.9545
3.	4	3, 2, 3	D2 + {1, 3, 4, 6, 7, 9, 10, 12}	0.9375	0.9740
4.	5	4, 2, 4	D3 + {1, 3, 4, 6, 7, 9, 10, 12}	0.9545	0.9825
5.	6	5, 3, 4	{1, 3, 4, 6, 7, 9, 10, 12} (4); {1, 2, 4, 5, 8, 9, 11, 12}; {2, 2, 5, 5, 8, 8, 11, 11}	0.9643	0.9853
6.	7	6, 3, 5	D5 + {1, 3, 4, 6, 7, 9, 10, 12}	0.9706	0.9885
7.	8	6, 4, 6	D6 + {1, 2, 4, 5, 8, 9, 11, 12}	0.9706	0.9880
8.	9	7, 4, 7	{1, 3, 4, 6, 7, 9, 10, 12} (6); {1, 2, 4, 5, 8, 9, 11, 12}; {2, 3, 5, 6, 7, 8, 10, 11}; {2, 2, 5, 5, 8, 8, 11, 11}	0.9750	0.9902
m = 4, *k* = 8					
9.	3	2, 1, 1, 2	{1, 4, 5, 8, 9, 12, 13, 16}; {1, 3, 5, 7, 10, 12, 14, 16}; {2, 4, 6, 8, 9, 11, 13, 15}	0.9706	0.9889
10.	4	2, 2, 2, 2	D9 + {2, 3, 6, 7, 10, 11, 14, 15}	0.9310	0.9726
11.	5	3, 2, 2, 3	D10 + {1, 4, 5, 8, 9, 12, 13, 16}	0.9800	0.9920
12.	6	4, 2, 2, 4	D11 + {1, 4, 5, 8, 9, 12, 13, 16}	0.9940	0.9978
13.	7	4, 3, 3, 4	D12 + {2, 3, 6, 7, 10, 11, 14, 15}	0.9844	0.9936
14.	8	5, 3, 3, 5	D13 + {1, 4, 5, 8, 9, 12, 13, 16}	0.9925	0.9971
15.	9	6, 3, 3, 6	D14 + {1, 4, 5, 8, 9, 12, 13, 16}	0.9966	0.9988

No.	*b*	p_u^{**}	Block contents	e_1	*e*
m = 5, *k* = 8					
16.	4	2, 2, 1, 1, 2	{1, 5, 6, 10, 11, 15, 16, 20}; {2, 4, 7, 9, 12, 14, 17, 19}; {1, 3, 6, 8, 13, 15, 18, 20}; {2, 5, 7, 10, 11, 14, 16, 19}	0.7857	0.9053
17.	5	3, 2, 1, 2, 2	D16 + {1, 4, 6, 9, 12, 15, 17, 20}	0.9176	0.9671
18.	6	3, 2, 2, 2, 3	D17 + {3, 5, 8, 10, 11, 13, 16, 18}	0.9519	0.9803
19.	7	4, 2, 2, 2, 4	D18 + {1, 5, 6, 10, 11, 15, 16, 20}	0.9684	0.9879
20.	8	4, 3, 2, 3, 4	D19 + {2, 4, 7, 9, 12, 14, 17, 19}	0.9560	0.9825
21.	9	5, 3, 2, 3, 5	D20 + {1, 5, 6, 10, 11, 15, 16, 20}	0.9721	0.9896
m = 6, *k* = 8					
22.	5	2, 2, 1, 1, 2, 2	{1, 6, 7, 12, 13, 18, 19, 24}; {2, 5, 8, 11, 14, 17, 20, 23}; {1, 4, 7, 10, 15, 18, 21, 24}; {2, 3, 8, 9, 16, 17, 22, 23}; {5, 6, 11, 12, 13, 14, 19, 20}	0.7606	0.8931
23.	6	3, 2, 1, 1, 2, 3	D22 + {1, 6, 7, 12, 13, 18, 19, 24}	0.7591	0.9008
24.	7	3, 2, 2, 2, 2, 3	D23 + {3, 4, 9, 10, 15, 16, 21, 22}	0.8143	0.9164
25.	8	3, 3, 2, 2, 3, 3	D24 + {2, 5, 8, 11, 14, 17, 20, 23}	0.8687	0.9426
26.	9	4, 3, 2, 2, 3, 4	D25 + {1, 6, 7, 12, 13, 18, 19, 24}	0.8850	0.9529
m = 7, *k* = 8					
27.	6	2, 2, 2, 1, 1, 2, 2	{1, 7, 8, 14, 15, 21, 22, 28}; {2, 6, 9, 13, 16, 20, 23, 27}; {3, 5, 10, 12, 17, 19, 24, 26}; {1, 4, 8, 11, 18, 21, 25, 28}; {2, 7, 9, 14, 15, 20, 22, 27}; {3, 6, 10, 13, 16, 19, 23, 26}	0.7632	0.8924
28.	7	3, 2, 2, 1, 2, 2, 2	D27 + {1, 5, 8, 12, 17, 21, 24, 28}	0.9146	0.9648
29.	8	3, 2, 2, 2, 2, 2, 3	D28 + {4, 7, 11, 14, 15, 18, 22, 25}	0.9491	0.9789
30.	9	3, 3, 2, 2, 2, 3, 3	D29 + {2, 6, 9, 13, 16, 20, 23, 27}	0.9587	0.9831
m = 4, *k* = 12					
31.	2	2, 1, 1, 2	{1, 2, 4, 5, 6, 8, 9, 11, 12, 13, 15, 16}; {1, 3, 4, 5, 7, 8, 9, 10, 12, 13, 14, 16}	0.9706	0.9889
32.	3	3, 2, 2, 2	D31 + {1, 2, 3, 5, 6, 7, 10, 11, 12, 14, 15, 16}	0.9696	0.9872
33.	4	4, 2, 2, 4	{1, 2, 4, 5, 6, 8, 9, 11, 12, 13, 15, 16} (2); {1, 3, 4, 5, 7, 8, 9, 10, 12, 13, 14, 16} (2)	0.9706	0.9889
34.	5	5, 3, 3, 4	D33 + {1, 2, 3, 5, 6, 7, 10, 11, 12, 14, 15, 16}	0.9752	0.9900
35.	6	6, 3, 3, 6	{1, 2, 4, 5, 6, 8, 9, 11, 12, 13, 15, 16} (3); {1, 3, 4, 5, 7, 8, 9, 10, 12, 13, 14, 16} (3)	0.9706	0.9889
m = 5, *k* = 12					
36.	3	2, 2, 1, 2, 2	{1, 3, 5, 6, 8, 10, 11, 13, 15, 16, 18, 20}; {1, 2, 4, 6, 7, 9, 12, 14, 15, 17, 19, 20}; {2, 4, 5, 7, 9, 10, 11, 12, 14, 16, 17, 19}	0.9494	0.9794

No.	b	p_u^{**}	Block contents	e_1	e
37.	4	3, 2, 2, 2, 3	D36 + {1, 3, 5, 6, 8, 10, 11, 13, 15, 16, 18, 20}	0.9706	0.9881
38.	5	4, 3, 2, 2, 4	D37 + {1, 2, 5, 6, 7, 10, 11, 14, 15, 16, 19, 20}	0.9716	0.9890
39.	6	5, 3, 2, 3, 5	D38 + {1, 4, 5, 6, 9, 10, 11, 12, 15, 16, 17, 20}	0.9718	0.9894
$m = 6,\ k = 12$					
40.	3	2, 2, 1, 1, 1, 2	{1, 2, 6, 7, 8, 12, 13, 17, 18, 19, 23, 24};	0.9878	0.9953
			{1, 4, 6, 7, 10, 12, 13, 15, 18, 19, 21, 24};		
			{2, 3, 5, 8, 9, 11, 14, 16, 17, 20, 22, 23}		
41.	4	3, 2, 1, 1, 2, 3	D40 + {1, 5, 6, 7, 11, 12, 13, 14, 18, 19, 20, 24}	0.9590	0.9854
42.	5	3, 3, 2, 2, 2, 3	D41 + {2, 3, 4, 8, 9, 10, 15, 16, 17, 21, 22, 23}	0.9540	0.9810
43.	6	4, 3, 2, 2, 3, 4	D41 + {1, 4, 6, 7, 10, 12, 13, 15, 18, 19, 21, 24};	0.9669	0.9872
			{2, 3, 5, 8, 9, 11, 14, 16, 17, 20, 22, 23}		
$m = 7,\ k = 12$					
44.	4	2, 2, 2, 1, 1, 2, 2	{1, 6, 7, 8, 13, 14, 15, 16, 21, 22, 23, 28};	0.9710	0.9885
			{2, 3, 6, 9, 10, 13, 16, 19, 20, 23, 26, 27};		
			{3, 4, 5, 10, 11, 12, 17, 18, 19, 24, 25, 26};		
			{1, 2, 7, 8, 9, 14, 15, 20, 21, 22, 27, 28}		
45.	5	3, 2, 2, 1, 2, 2, 3	{1, 4, 7, 8, 11, 14, 15, 18, 21, 22, 25, 28};	0.9851	0.9944
			{2, 3, 6, 9, 10, 13, 16, 19, 20, 23, 26, 27};		
			{1, 5, 7, 8, 12, 14, 15, 16, 17, 20, 23, 24, 28};		
			{1, 3, 7, 8, 10, 14, 15, 19, 21, 22, 24, 28};		
			{2, 5, 6, 9, 12, 13, 17, 19, 23, 24, 26}		
46.	6	3, 3, 2, 2, 2, 3, 3	D45 + {2, 4, 6, 9, 11, 13, 16, 18, 20, 23, 25, 27}	0.9559	0.9819
$m = 8,\ k = 12$					
47.	4	2, 2, 1, 1, 1, 1, 2, 2	{1, 4, 8, 9, 12, 16, 17, 21, 24, 25, 29, 32};	0.9809	0.9926
			{2, 3, 7, 10, 11, 15, 18, 22, 23, 26, 30, 31};		
			{1, 6, 8, 9, 14, 16, 17, 19, 24, 25, 27, 32};		
			{2, 5, 7, 10, 13, 15, 18, 20, 23, 26, 28, 31}		
48.	5	3, 2, 2, 1, 1, 2, 2, 2	{1, 4, 8, 9, 12, 16, 17, 21, 24, 25, 29, 32};	0.9810	0.9926
			{2, 3, 7, 10, 11, 15, 18, 22, 23, 26, 30, 31};		
			{1, 3, 6, 9, 11, 14, 19, 22, 24, 27, 30, 32};		
			{1, 5, 8, 9, 13, 16, 17, 20, 24, 25, 28, 32};		
			{2, 5, 7, 10, 13, 15, 18, 20, 23, 26, 28, 31}		
49.	6	3, 2, 2, 2, 2, 2, 2, 3	D48 + {4, 5, 8, 12, 13, 16, 17, 20, 21, 25, 28, 29}	0.9704	0.9878
$m = 5,\ k = 16$					
50.	2	2, 1, 1, 2, 2	{1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20};	0.9900	0.9961
			{1, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 15, 16, 17, 19, 20}		
51.	3	3, 2, 2, 2, 3	{1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20} (2);	1.0000	1.0000
			{1, 3, 3, 5, 6, 8, 8, 10, 11, 13, 13, 15, 16, 18, 18, 20}		

No.	*b*	p_u^{**}	Block contents	e_1	*e*
52.	4	4, 3, 2, 3, 4	{1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20} (3); {1, 3, 3, 5, 6, 8, 8, 10, 11, 13, 13, 15, 16, 18, 18, 20}	1.0000	1.0000
m = 6, *k* = 16					
53.	3	3, 2, 1, 1, 2, 3	{1, 2, 5, 6, 7, 8, 11, 12, 13, 14, 17, 18, 19, 20, 23, 24} (2); {1, 3, 4, 6, 7, 9, 10, 12, 13, 15, 16, 18, 19, 21, 22, 24}	1.0000	1.0000
54.	4	3, 3, 2, 2, 3, 3	D53 + {2, 3, 4, 5, 8, 9, 10, 11, 14, 15, 16, 17, 20, 21, 22, 23}	1.0000	1.0000
m = 7, *k* = 16					
55.	3	2, 2, 2, 1, 1, 2, 2	{1, 2, 6, 7, 8, 9, 13, 14, 15, 16, 20, 21, 22, 23, 27, 28}; {1, 3, 5, 7, 8, 10, 12, 14, 15, 17, 19, 21, 22, 24, 26, 28}; {2, 3, 4, 6, 9, 10, 11, 13, 16, 18, 19, 20, 23, 25, 26, 27}	0.9943	0.9978
56.	4	3, 2, 2, 2, 2, 2, 3	{1, 2, 6, 7, 8, 9, 13, 14, 15, 16, 20, 21, 22, 23, 27, 28} (2); {1, 3, 5, 7, 8, 10, 12, 14, 15, 17, 19, 21, 22, 24, 26, 28}; {3, 4, 4, 5, 10, 11, 11, 12, 17, 18, 18, 19, 24, 25, 25, 26}	1.0000	1.0000
m= 8, *k* = 16					
57.	3	2, 2, 1, 1, 1, 1, 2, 2	{1, 2, 7, 8, 9, 10, 15, 16, 17, 18, 23, 24, 25, 26, 31, 32}; {1, 4, 5, 8, 9, 12, 13, 16, 17, 20, 21, 24, 25, 28, 29, 32}; {2, 3, 6, 7, 10, 11, 14, 15, 18, 19, 22, 23, 26, 27, 30, 31}	1.0000	1.0000
58.	4	3, 2, 2, 1, 1, 2, 2, 3	D57 + {1, 3, 6, 8, 9, 11, 14, 16, 17, 19, 22, 24, 25, 27, 30, 32}	1.0000	1.0000

Table 2. *A*-optimal block designs (disconnected) with c = 3, 3 ≤ m ≤ 8, k = 8, k < 4m, bk ≤ 75

No.	*b*	p_u^{**}	Block contents
m = 3			
1.	3	2, 2, 2	{1, 3, 4, 6, 7, 9, 10, 12}(2); {2, 2, 5, 5, 8, 8, 11, 11}
2.	4	3, 2, 3	{1, 3, 4, 6, 7, 9, 10, 12}(3); {2, 2, 5, 5, 8, 8, 11, 11}
3.	5	4, 2, 4	{1, 3, 4, 6, 7, 9, 10, 12}(4); {2, 2, 5, 5, 8, 8, 11, 11}
4.	8	6, 4, 6	{1, 3, 4, 6, 7, 9, 10, 12}(6); {2, 2, 5, 5, 8, 8, 11, 11} (2)
5.	9	7, 4, 7	{1, 3, 4, 6, 7, 9, 10, 12}(7); {2, 2, 5, 5, 8, 8, 11, 11} (2)
m = 4			
6.	3	2, 1, 1, 2	{1, 4, 5, 8, 9, 12, 13, 16}(2); {2, 3, 6, 7, 10, 11, 14, 15}
7.	4	2, 2, 2, 2	{1, 4, 5, 8, 9, 12, 13, 16}(2); {2, 3, 6, 7, 10, 11, 14, 15} (2)
8.	5	3, 2, 2, 3	{1, 4, 5, 8, 9, 12, 13, 16}(3); {2, 3, 6, 7, 10, 11, 14, 15} (2)
9.	6	4, 2, 2, 4	{1, 4, 5, 8, 9, 12, 13, 16}(4); {2, 3, 6, 7, 10, 11, 14, 15} (2)
10.	7	4, 3, 3, 4	{1, 4, 5, 8, 9, 12, 13, 16}(4); {2, 3, 6, 7, 10, 11, 14, 15} (3)
11.	8	5, 3, 3, 5	{1, 4, 5, 8, 9, 12, 13, 16}(5); {2, 3, 6, 7, 10, 11, 14, 15} (3)
12.	9	6, 3, 3, 6	{1, 4, 5, 8, 9, 12, 13, 16}(6); {2, 3, 6, 7, 10, 11, 14, 15} (3)
m = 5			
13.	6	3, 2, 2, 2, 3	{1, 5, 6, 10, 11, 15, 16, 20}(3); {2, 4, 7, 9, 12, 14, 17, 19} (2);{3, 3, 8, 8, 13, 13, 18, 18}
14.	7	4, 2, 2, 2, 4	{1, 5, 6, 10, 11, 15, 16, 20}(4); {2, 4, 7, 9, 12, 14, 17, 19} (2); {3, 3, 8, 8, 13, 13, 18, 18}
15.	8	4, 3, 2, 3, 4	{1, 5, 6, 10, 11, 15, 16, 20}(4); {2, 4, 7, 9, 12, 14, 17, 19} (3); {3, 3, 8, 8, 13, 13, 18, 18}
16.	9	5, 3, 2, 3, 5	{1, 5, 6, 10, 11, 15, 16, 20}(5); {2, 4, 7, 9, 12, 14, 17, 19} (3); {3, 3, 8, 8, 13, 13, 18, 18}
m = 6			
17.	5	2, 2, 1, 1, 2, 2	{1, 6, 7, 12, 13, 18, 19, 24} (2); {2, 5, 8, 11, 14, 17, 20, 23} (2); {3, 4, 9, 10, 15, 16, 21, 22}
18.	6	3, 2, 1, 1, 2, 3	{1, 6, 7, 12, 13, 18, 19, 24} (3); {2, 5, 8, 11, 14, 17, 20, 23} (2); {3, 4, 9, 10, 15, 16, 21, 22}
19.	7	3, 2, 2, 2, 2, 3	{1, 6, 7, 12, 13, 18, 19, 24} (3); {2, 5, 8, 11, 14, 17, 20, 23} (2); {3, 4, 9, 10, 15, 16, 21, 22} (2)
20.	8	3, 3, 2, 2, 3, 3	{1, 6, 7, 12, 13, 18, 19, 24} (3); {2, 5, 8, 11, 14, 17, 20, 23} (3); {3, 4, 9, 10, 15, 16, 21, 22} (2)
21.	9	4, 3, 2, 2, 3, 4	{1, 6, 7, 12, 13, 18, 19, 24}(4); {2, 5, 8, 11, 14, 17, 20, 23} (3); {3, 4, 9, 10, 15, 16, 21, 22} (2)
m = 7			
22.	8	3, 2, 2, 2, 2, 2, 3	{1, 7, 8, 14, 15, 21, 22, 28} (3); {2, 6, 9, 13, 16, 20, 23, 27} (2); {3, 5, 10, 12, 17, 19, 24, 26} (2); {4, 4, 11, 11, 18, 18, 25, 25}
23.	9	3, 3, 2, 2, 2, 3, 3	{1, 7, 8, 14, 15, 21, 22, 28} (3); {2, 6, 9, 13, 16, 20, 23, 27} (3); {3, 5, 10, 12, 17, 19, 24, 26} (2); {4, 4, 11, 11, 18, 18, 25, 25}