

Efficient Block Designs for 2-Colour Microarray Experiments

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SUMMARY

This article deals with the problem of obtaining efficient designs for 2-colour microarray experiments. If arrays are considered as blocks and varieties as treatments and the number of varieties that can be accommodated on each array as block size, then a classical incomplete block design can be useful for microarray experiments. Since only two varieties can be accommodated on one array in 2-colour microarray experiment, effects due to arrays may be considered as random. To deal with the problem of obtaining an efficient design when array effects are random, lower bounds to A- and D-efficiencies of the design in a given class of designs have been obtained for block designs under a mixed effects model. For obtaining efficient block designs under fixed/mixed effects model for microarray experiments, the exchange and interchange algorithm of Rathore *et al.* (2006) was modified by incorporating the procedure of computing lower bounds to A- and D-efficiencies under a mixed effects model. The algorithm has been translated into a computer program using Microsoft Visual C++. The algorithm is general in nature and can be used for generation of efficient block design for any $2 \leq k < v$, where v is the number of varieties (treatments) and k is the block size. The algorithm has been exploited for computer aided search of an efficient block design in v varieties and b -arrays for two colour micro-array experiments ($k = 2$) in the parametric range $3 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and $17 \leq v = b \leq 25$. Designs obtained through the algorithm under fixed effects model have been compared with the corresponding best designs available in the literature (designs with highest lower bound to A-efficiency) and 2-associate partially balanced incomplete block {PBIB(2)} designs. 30 designs are found to be more efficient than the best available block designs. The robustness aspects of efficient designs obtained under a fixed effects model and best available block designs were investigated under mixed effects model. Strength of the algorithm for obtaining block designs for 3-colour microarray experiments has also been demonstrated with the help of examples.

Key words : Microarray experiments, Mixed effects model, A-efficiency, D-efficiency.

1. INTRODUCTION

Microarrays are microscopic arrays of single-stranded deoxyribonucleic acid (DNA) molecules immobilized on a solid surface by biochemical synthesis. These are also known as DNA chips, gene chips, biochips, DNA microarrays or simply the arrays. Microarray is an important genomics tool that can identify the expression of several thousand genes at a time. The basic idea behind microarray technology is to simultaneously measure the relative expression level of thousands of genes within a particular cell population or

tissue. In 2-colour microarray experiments, samples of DNA clones (or probes) with known sequence content are spotted and immobilized onto a glass slide or other substrate called "microarray" so that each spot in the microarray corresponds to a gene or an expressed sequence tag (EST). This is followed by reverse transcription of pools of purified messenger ribonucleic acid (mRNA) from cell populations (henceforth called as varieties) into complementary DNA (cDNA) and labelled with one of two fluorescent dyes, red or green. In microarray technology, the "red" and "green" signals/fluorescence readings/intensity from a spot indicate the relative abundance of the corresponding mRNA in the

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two cell populations which are taken as response variable in microarray experiments. The details about microarray experiments can be obtained in Gupta *et al.* (1999), Sebastiani *et al.* (2003), Chawla (2003), Datta (2003), Kerr (2003) and Lee (2004).

In a microarray experiment, four basic experimental factors viz., array (A), dye (D), variety (V) and gene (G) are studied. These four factors give rise to 15 effects that include 4 main effects, 6 two-factor interactions, 4 three-factor interactions and one four-factor interaction. But all the main effects and selected two-factor interactions viz., array-gene interaction (AG), dye-gene interaction (DG), variety-gene interaction (VG) are the seven effects of interest to the experimenter. In the present investigation we consider a situation where same set of genes is spotted on each array in microarray experiments. Therefore, genes/gene specific effects (G, AG, DG, VG) are orthogonal to global effects (A, D, V). Therefore, optimality aspects of designs for microarray experiments can be studied by taking only array, dye and variety effects and leaving gene specific effects from the model. Designs that are efficient under the model containing only global effects are also efficient under the model containing both global and gene specific effects.

The commonly used designs in microarray experiments are reference sample design (Kerr and Churchill, 2001a; Yang and Speed, 2002), alternating loop design (Kerr and Churchill, 2001b; Yang and Speed, 2002) and dye-swap design (Kerr and Churchill, 2001a; Yang and Speed, 2002). Optimal/efficient designs for microarray experiments have been obtained under a restricted fixed effects model containing only array and variety effects in the model ignoring the dye effects. Dye effects have been assumed to be orthogonal to variety effects. Further, in 2-colour microarray experiments only two varieties labelled with two different dyes can be accommodated on one array. If we consider arrays as blocks and varieties as treatments, then the designs for microarray experiments are block designs with 2 plots per block.

Kerr and Churchill (2001a), Yang (2003) and Nguyen and Williams (2005) studied optimality aspects of designs for two-colour microarray experiments under a 2-plot block design setup. Kerr and Churchill (2001a) used non-isomorphic connected graphs on v vertices using Brendan McKay's, MAKEG program and

compared all designs of the same size $D(v, b)$ on the basis of A-optimality under the model containing only array and variety effects in the model. They catalogued A-optimal designs and best even designs (a design is an even design when replication of each variety is even and is best when the lower bound to A-efficiency is highest among the designs available in the literature) for block size two, number of varieties $6 \leq v \leq 10$ and number of arrays $v \leq b \leq v(v-1)/2$. They have also catalogued A-optimal designs for $(v, b) = (11, 13), (12, 14), (13, 14)$ and $(13, 15)$. Their search of all possible designs becomes computationally infeasible for larger v . The concurrence matrices of the designs are available at <http://www.jax.org/staff/churchill/labsite/pubs/index.html>. Yang (2003) studied A-optimality aspects under the same restricted model and used algorithm by Tjur (1993) to search A-optimal designs when $3 \leq v = b \leq 25$. Loop designs were A-optimal for $3 \leq v \leq 8$; Mix(4) designs were A-optimal for $9 \leq v \leq 12$ and Mix(3) designs were A-optimal for $12 \leq v \leq 25$ under restricted model. A Mix(i) design is a mixture of a loop design (of length i) and a reference design. Nguyen and Williams (2005) obtained efficient block designs under the same restricted model for $6 \leq v \leq 20$ and $v \leq b \leq v(v-1)/2$. The designs are available at <http://mcs.une.edu.au/~nkn/mad/>. These three catalogues contain some overlapping designs. Therefore, it is required to identify/obtain a design for given parameters, which makes all the possible pairwise treatment comparisons under a fixed effects model with as high a precision as possible (high A- and D-efficiencies). Sarkar and Parsad (2006) made a comprehensive review of the designs for 2-colour microarray experiments and prepared a catalogue of 562 most A-efficient designs available in the literature (henceforth called as best available designs) along with their lower bounds to A- and D-efficiencies for $3 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and $17 \leq v = b \leq 25$.

All these studies, however, are restricted to a fixed effects model. As described earlier, only 2 varieties can be accommodated on each array and each array has to be prepared separately. Therefore, Kerr and Churchill (2001a), Wolfinger *et al.* (2001), Lee (2004) have remarked that array effects should be taken as random. When array effects are random, then the usual model of a block design set up is a two-way classified, additive, mixed effects linear model. It may be of interest to

investigate “whether a design that is optimal/efficient under a fixed effects model remains optimal/efficient under a mixed effects model?”. Therefore, there is a need to study the optimality aspects of designs under a mixed effects model. It is also required to investigate the robustness of designs (efficient under a fixed effects model) when array effects are random. There are two approaches of handling the above problem.

Approach 1. Obtain an efficient design under a mixed effects model for a given value of ρ , a function of inter and intra block variances. Since ρ is generally unknown, there is a need to study the robustness of the design under varying values of ρ .

Approach 2. Obtain an efficient design under fixed effects model ($\rho = 0$) and study the behaviour of the A-efficiencies of this design under mixed effects model for different values of $\rho = 0.1, 0.2, 0.3, 0.4, \dots, 0.9$.

In the present investigation, approach 2 has been used, although some description and problem of obtaining efficient designs using approach 1 is also given in Section 8.

The present investigation modifies the algorithm of Rathore *et al.* (2006) for computer aided search of A- and D-efficient designs for 2-colour microarray experiments in which only two varieties labelled with two different dyes can be accommodated on one array and arrays are blocks of size 2 each. The array effects are treated as random. In Section 3, we have obtained expressions for lower bounds to A- and D-efficiency of block designs under a mixed effects model. The lower bounds to A- and D-efficiencies of block designs under mixed effects model have been incorporated in the exchange and interchange algorithm of Rathore *et al.* (2006). The modified algorithm is discussed in Section 4. This algorithm was converted into a VC++ code for computer aided search of efficient designs. In Section 5 this algorithm and VC++ code was used for computer aided search of efficient block designs for making all possible pairwise variety comparisons for 2-colour microarray experiments for $3 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and $17 \leq v = b \leq 25$, respectively.

The designs obtained through computer aided search are then compared with best available block designs as given in Sarkar and Parsad (2006). For given v , b and block size 2, the unreduced balanced incomplete block

(BIB) design with $b = v(v-1)/2$ is optimal according to a wide family of criteria and can be used for 2-colour microarray experiments. These designs, however, require a large number of arrays. It is, therefore, worthwhile examining if partially balanced incomplete block designs with two associate classes [PBIB(2) designs] could be used as designs for microarray experiments if their A-efficiency is high. We also made a comparison of the designs obtained and best available design with those of PBIB(2) designs catalogued in Clatworthy (1973). The results obtained are discussed in Section 5. The two varieties in each array are to be labelled with two dyes. If we take that the variety appearing in position 1 is labelled with dye 1 and that at position 2 is labelled with dye 2, then it is of utmost importance to rearrange the block contents in such a fashion that the varieties are most balanced with respect to dyes. In all the catalogues prepared, effort has been made that the block contents are such that the varieties are most balanced with respect to dyes.

We have already emphasized that there is a need to study optimality aspects of designs for microarray experiments under mixed effects model considering array effects as random. We study this by working out the lower bounds to A- and D-efficiencies of the designs. The expressions for lower bounds to A- and D-efficiencies would depend on ρ , a function of intra and inter block variances. ρ is generally unknown and lies between 0 and 1. Further, a design which is efficient for a given value of ρ may not be so for other values of ρ . Therefore, it is desirable to study the variation in lower bound to A-[D-] efficiencies for different values of ρ . We obtain an efficient design under a fixed effects model and compute lower bounds to A-[D-] efficiencies for $0.0 \leq \rho \leq 0.9$ and obtain percent Coefficient of Variation (CV) in A-efficiencies for both the design obtained through algorithm and also for the best available block design for the given set of parameters. If CV is small, then we say that the design is robust against the values of ρ and can be used for any value of ρ . The robustness aspects of the designs are studied in Section 6.

The above description is for 2-colour microarray experiments. Recently three- and four-colour microarrays have also been proposed in the literature (Woo *et al.* 2005). The modified algorithm used in the present investigation is general in nature and helps

generate efficient block design for block size $2 \leq k < v$. Some efficient designs for 3-colour microarray experiments are given in Section 7. Finally, the procedure of obtaining an efficient design for a given value of $\rho (> 0)$ and its robustness against other values of $0.0 \leq \rho \leq 0.9$ is described in Section 8. We begin with some preliminaries of block designs in Section 2.

2. PRELIMINARIES OF BLOCK DESIGNS

We begin with some preliminaries about a general block design. We shall assume the usual two-way classified, linear, mixed effects, additive model considering block (array) effects as random.

Consider a block design $d \in D(v, b, \mathbf{r}, \mathbf{k}, \mathbf{N}, \mathbf{w})$ where \mathbf{D} denotes the class of connected block designs with v treatments arranged in b blocks with a v -component vector of replications $\mathbf{r}' = (r_1, \dots, r_v)$, and b -component vector of block sizes $\mathbf{k}' = (k_1, \dots, k_b)$; \mathbf{N} is the $v \times b$ incidence matrix of treatments versus blocks with elements as n_{hj} ($h = 1, \dots, v, j = 1, \dots, b$) where integer $n_{hj} (\geq 0)$ denotes the replication of h^{th} treatment in j^{th} block. A design is binary if $n_{hj} = 0$ or 1. The linear mixed effects model is

$$\mathbf{y} = \mathbf{1}\mu + \mathbf{A}'\boldsymbol{\tau} + \mathbf{D}'\boldsymbol{\beta} + \boldsymbol{\varepsilon}$$

where,

\mathbf{y} is $n \times 1$ vector of observations

μ is the general mean effect

$\boldsymbol{\tau}$ is the $v \times 1$ vector of treatment effects

$\boldsymbol{\beta}$ is the $b \times 1$ random vector of block effects

$\boldsymbol{\varepsilon}$ is the $n \times 1$ random vector of error components

Further, $\text{Cov}(\boldsymbol{\beta}, \boldsymbol{\varepsilon}) = \mathbf{0}$. We also assume that

$$\boldsymbol{\beta} \sim N(\mathbf{0}, \sigma_{\beta}^2 \mathbf{I}_b) \text{ and } \boldsymbol{\varepsilon} \sim N(\mathbf{0}, \sigma^2 \mathbf{I}_n), \text{ where } \sigma_{\beta}^2 \text{ and } \sigma^2$$

are unknown variance parameters for block effects and error respectively. $\mathbf{W} = \text{diag}(w_1, \dots, w_b)$ is a diagonal

matrix with diagonal elements $w_j = \sigma_{\beta}^2 / (\sigma^2 + k_j \sigma_{\beta}^2)$

$\forall j = 1, \dots, b$.

Let $\mathbf{R} = \text{diag}(r_1, \dots, r_v)$ and $\mathbf{K} = \text{diag}(k_1, \dots, k_b)$ denote respectively the diagonal matrices of replications

and block sizes and $n = \sum_{j=1}^b k_j = \sum_{h=1}^v r_h$ be the total number of observations in the design. Using the principle of generalized least squares, the coefficient matrix of reduced normal equations for obtaining the Best Linear Unbiased Estimates (BLUE) of estimable linear functions of treatment effects is

$$\mathbf{C} = \mathbf{R} - \mathbf{N}\mathbf{W}\mathbf{N}' - (\mathbf{r} - \mathbf{N}\mathbf{W}\mathbf{k})(\mathbf{n} - \mathbf{k}'\mathbf{W}\mathbf{k})^{-1}(\mathbf{r} - \mathbf{N}\mathbf{W}\mathbf{k}) \quad (2.1a)$$

For a binary proper block design, $k_j = k \forall j = 1, \dots, b$ and then the coefficient matrix of reduced normal equations in (2.1a) reduces to

$$\mathbf{C} = \mathbf{R} - \frac{1}{k}\mathbf{N}\mathbf{N}' + \rho \left(\frac{1}{k}\mathbf{N}\mathbf{N}' - \frac{1}{bk}\mathbf{r}\mathbf{r}' \right) \quad (2.1b)$$

where

$$\rho = (1 - kw) = \frac{\sigma^2}{(\sigma^2 + k\sigma_{\beta}^2)}$$

$\rho = 0$ corresponds to the usual fixed effects model. Generally ρ is unknown. We obtain a design under a fixed effects model and study the robustness of the most efficient design for $\rho = 0$ against the variation in the values of ρ in the range $0 \leq \rho \leq 0.9$. In other words, the lower bound to the A-efficiency of the most efficient design for $\rho = 0$ is obtained for all the designs for values of ρ in the range $0 \leq \rho \leq 0.9$. If the percent coefficient of variation (CV) of the lower bound to A-efficiencies is small, then the most efficient design for $\rho = 0$ is robust. In that case, we may use this design for any value of ρ in the range $0.1 \leq \rho \leq 0.9$.

For the usual fixed effects model, the coefficient matrix of reduced normal equations given in (2.1a) reduces to

$$\mathbf{C} = \mathbf{R} - \mathbf{N}\mathbf{K}^{-1}\mathbf{N}'$$

The $v \times v$ \mathbf{C} -matrices in (2.1a), (2.1b) and (2.1c) are symmetric, positive semi-definite and have row sums equal to zero. For a connected block design, $\text{Rank}(\mathbf{C}) = v - 1$. We shall study connected designs only. Let \mathbf{C}^- be a generalized inverse of \mathbf{C} matrix *i.e.* $\mathbf{C}\mathbf{C}^-\mathbf{C} = \mathbf{C}$. Let $\mathbf{p}'\boldsymbol{\tau}$ be an estimable parametric function

of treatment effects, where τ is a v -component vector of treatment effects. Let $\mathbf{p}'\hat{\tau}$ denote the BLUE of $\mathbf{p}'\tau$, where $\hat{\tau}$ is any solution of the normal equations. Variance of $\mathbf{p}'\hat{\tau}$ is $\text{var}(\mathbf{p}'\hat{\tau}) = (\mathbf{p}'\mathbf{C}^{-1}\mathbf{p})\sigma^2$.

Suppose now that the interest of the experimenter is in estimating several parametric functions, each parametric function being estimated with a different (known) weight. The problem then reduces to obtain BLUE of

$$\mathbf{P}'\tau = \begin{bmatrix} \mathbf{p}'_1\tau \\ \mathbf{p}'_2\tau \\ \vdots \\ \mathbf{p}'_s\tau \end{bmatrix}$$

where \mathbf{P}' is a $s \times v$ matrix and the rows of \mathbf{P}' are estimable parametric functions, through a design d that minimizes

$$\begin{aligned} T_d &= \sum_{i=1}^s \omega_i \text{var}(\mathbf{p}'_i\hat{\tau}) \\ &= \sigma^2 \text{trace}(\mathbf{\Omega P}'\mathbf{C}^{-1}\mathbf{P}) \end{aligned} \tag{2.2}$$

This is weighted A-optimality studied earlier by Freeman (1976) and $\mathbf{\Omega} = \text{diag}(w_1, \dots, w_s)$; w_i being the weight associated with the i^{th} parametric function, $i = 1, 2, \dots, s$.

In the context of microarray experiments we are interested in all the possible pairwise comparisons of varieties and, therefore, $s = {}^v C_2$. It may be noted that for $s = {}^v C_2$, $\mathbf{P}\mathbf{P}' = v\mathbf{I} - \mathbf{1}\mathbf{1}'$; $\mathbf{P}'\mathbf{P} = \mathbf{I}_{v-1}$. Further, if comparisons among treatments are made with the same precision, then $\mathbf{\Omega} = \mathbf{I}_s$ and (2.2) can be rewritten as

$$\begin{aligned} \sigma^{-2}T_d &= \text{trace}(\mathbf{P}'\mathbf{C}^{-1}\mathbf{P}) = \text{trace}(\mathbf{C}^{-1}\mathbf{P}\mathbf{P}') \\ &= \text{trace}(\mathbf{C}^+\mathbf{P}\mathbf{P}') \end{aligned}$$

where \mathbf{C}^+ is the Moore-Penrose g -inverse of \mathbf{C} . Further, if $s = {}^v C_2$, then $\sigma^{-2}T_d = \text{trace}(v\mathbf{C}^+)$.

Let $\mathbf{D} = \mathbf{D}(v, b, k, \rho)$ denote the class of connected proper block designs with block effects as random and given ρ in which v treatments are arranged in b blocks each of size k . A design $d^* \in \mathbf{D}$ is said to be A-optimal if $T_{d^*} = \min(T_d)$, $d \in \mathbf{D}$. Similarly a design $d^* \in \mathbf{D}$ is said to be D-optimal if it minimizes the determinant of the variance-covariance matrix $\mathbf{P}'\mathbf{C}^{-1}\mathbf{P}$ over all $d \in \mathbf{D}$.

3. LOWER BOUNDS TO A- AND D-EFFICIENCY OF BLOCK DESIGNS UNDER MIXED EFFECTS MODEL

In this section, we shall obtain the expressions for lower bounds to A-[D-] efficiencies under a mixed effects model. The problem of obtaining an A-[D-] optimal design for making all possible pairwise treatment comparisons is equivalent to the problem of obtaining an A-[D-] optimal design for a complete set of orthonormalized treatment contrasts $\mathbf{P}'\tau$. Define

$$\phi_A(d) = \sum_{i=1}^{v-1} \theta_i^{-1} \quad \text{and} \quad \phi_D(d) = \prod_{i=1}^{v-1} \theta_i^{-1} \quad \text{where}$$

$\theta_1, \theta_2, \dots, \theta_{v-1}$ are the non-zero eigenvalues of \mathbf{C} . Then, a design d is A- [D-] optimal for inferring on a complete set of orthonormalized treatment contrasts if it minimizes $\phi_A(d)[\phi_D(d)]$ over \mathbf{D} .

The A-efficiency $\{e_A(d)\}$ and D-efficiency $\{e_D(d)\}$ of any design d over \mathbf{D} is defined as

$$e_A(d) = \frac{\phi_A(d_A^*)}{\phi_A(d)} \quad \text{and} \quad e_D(d) = \left[\frac{\phi_D(d_D^*)}{\phi_D(d)} \right]^{1/(v-1)}$$

where d_A^* and d_D^* are the hypothetical A-optimal and D-optimal designs over \mathbf{D} , respectively.

Using the following inequality by Shah and Sinha (1989)

$$\sum_{i=1}^{v-1} f(\theta_i) \geq \frac{v-1}{v} \sum_{h=1}^v f\left(\frac{v}{v-1} C_{hh}\right) \tag{2.4}$$

where f is convex and assumed to be non-increasing over $[0, \infty)$. Now using arithmetic mean, geometric mean, harmonic mean inequality on diagonal elements of \mathbf{C} , the lower bounds to A-efficiency and D-efficiency for a connected proper block design $d \in \mathbf{D}$ are given by

$$\begin{aligned} e_A(d) &= \frac{(v-1)^2}{\{b(k-1) + \rho b(1-k/v)\} \phi_A(d)} \\ e_D(d) &= \frac{(v-1)}{\{b(k-1) + \rho b(1-k/v)\} \{\phi_D(d)\}^{1/(v-1)}} \end{aligned}$$

Remark 3.1. For $\rho = 0$, the mixed effects model reduces to the usual fixed effects model and the class of designs $\mathbf{D}(v, b, k, \rho)$ will be denoted by $\mathbf{D}(v, b, k)$. The lower bounds to A- and D-efficiencies reduce to

$$e_A(d) = \frac{(v-1)^2}{b(k-1)\phi_A(d)} \text{ and}$$

$$e_D(d) = \frac{(v-1)}{b(k-1)\{\phi_D(d)\}^{1/(v-1)}}$$

These expressions were obtained earlier by Rathore *et al.* (2006).

4. ALGORITHM BASED ON EXCHANGE AND INTERCHANGE OF TREATMENTS

Rathore *et al.* (2006) modified the algorithm of Jones and Eccleston (1980) for computer aided search of efficient proper block designs under fixed effects model. Our aim is to obtain optimal/efficient block designs with block size 2 under fixed effects model as well as to study their robustness under mixed effects model. We modify the algorithm of Rathore *et al.* (2006) to obtain optimal/ efficient block designs under a fixed effects model that are robust under a mixed effects model. In fact the modification is in term of step 6. The first 5 steps are same as given in Rathore *et al.* (2006). The broad outline of the modified algorithm is described in the sequel.

1. Generate a binary block design for given parameters randomly; only values of v (number of treatments), b (number of blocks) and k (block size) are required as input to routine. This selection of random design is key to success and should be done with proper care. The starting design should be binary and connected. A design is connected if the determinant of $[C + (1/v)11']$ is non-zero. The C -matrix used here is as given in (2.1c). The algorithm selects the starting design in two ways *viz.* (i) with full randomization and (ii) by fixing the replication of the treatments. These are described later.
2. Now employ exchange procedure as explained by Jones and Eccleston (1980). In this step weakest observation is replaced by the strongest observation. The exchange procedure is continued until no further improvement is made in the design in terms of the criterion used.
3. After the termination of exchange steps we apply the procedure of treatments interchange. In this process a pair of treatments whose interchange yields

an improvement with respect to optimality criterion is interchanged.

4. After termination of Step 3 we obtain lower bounds to A- and D-efficiencies of the final design obtained using expressions (2.7).
5. If the efficiency of the design is not satisfactory, the whole procedure is repeated by selecting a new starting design randomly. This procedure is continued till a design with satisfactory efficiency is obtained. In the present investigation, all the designs are obtained with maximum of 3 to 4 random starts.
6. The A- and D-efficiencies of the final design obtained in Step 5 are computed for different values of ρ *viz.* $0 \leq \rho \leq 0.9$ using the C -matrix given in (2.1b) and the expressions (2.5) and (2.6) and per cent Coefficient of Variation (CV) of the efficiencies for different values of ρ , $0 \leq \rho \leq 0.9$ is computed.

If the CV is small, then we say that the design is robust and can be used for any value of ρ . The algorithm is general in nature and can be used for obtaining efficient block designs for any block size $2 \leq k < v$. In the present investigation, this algorithm has been exploited only for $k = 2$.

5. EFFICIENT BLOCK DESIGNS FOR MICROARRAY EXPERIMENTS

Using the algorithm described in Section 4, we have made a computer aided search of block designs with block size 2 for making all possible pairwise treatment comparisons under fixed effects model for $3 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and for $17 \leq v = b \leq 25$.

A total of 569 designs have been obtained in the above parametric range. The designs generated have been divided into two parts: the first part contains 562 designs for those parametric combinations for which designs are also available in the literature and 7 designs for those parametric combinations for which no design is catalogued in the literature on microarrays. All these designs along with block contents and lower bounds to A- and D-efficiencies are available with the first author and can be obtained by sending an E-mail to ananta8976@gmail.com.

Out of the 569 designs, 14 parametric combinations correspond to unreduced BIB designs for

$v = 3, 4, \dots, 16$ and the algorithm has generated all these unreduced BIB designs.

5.1 Comparison with Best Available Designs for Microarray Experiments

Kerr and Churchill (2001a), Yang (2003) and Nguyen and Williams (2005) prepared catalogues of efficient block designs for microarray experiments. The details of the parametric combinations studied by these authors are given in Section 1. As mentioned earlier, for $3 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and $17 \leq v = b \leq 25$, Sarkar and Parsad (2006) gave a comprehensive catalogue of 562 best available designs along with lower bounds to A- and D-efficiencies.

The designs obtained in the present investigation are compared with the best available designs (designs with highest lower bound to A-efficiency) and catalogued in Sarkar and Parsad (2006). Table 5.1 below gives the frequency of designs generated by the algorithm that are more efficient, equally efficient and less efficient than the best available designs in different parametric ranges.

30 designs have been found to be more efficient, 394 designs to be equally efficient and 138 designs to be

less efficient than the best available designs. The results are for the designs obtained in the computer aided search. It may, however, be possible to find a design at least as efficient as the best available design through further computer aided search. For illustration we give two designs which have more A-efficiencies than the corresponding best available designs. For example, for $v = 9, b = 25$, the best available design and the design obtained are

D1: Best Available Design

(7, 1); (6, 3); (2, 1); (4, 8); (1, 4); (7, 2); (8, 5);
 (3, 5); (9, 7); (2, 6); (8, 9); (9, 6); (5, 6); (6, 1);
 (2, 3); (8, 2); (3, 9); (1, 8); (9, 4); (4, 7); (4, 5);
 (1, 3); (5, 7); (5, 2); (3, 4)

Lower Bound to A-Efficiency = 0.9480
 Lower Bound to D-Efficiency = 0.9607

D2: Design Obtained

(3, 7); (4, 9); (5, 3); (6, 9); (8, 4); (8, 6); (5, 8);
 (7, 2); (6, 3); (6, 1); (4, 7); (5, 7); (2, 4); (3, 4);
 (2, 6); (1, 3); (1, 2); (9, 5); (7, 8); (8, 1); (7, 9);
 (4, 6); (9, 1); (2, 5); (1, 5)

Lower Bound to A-Efficiency = 0.9515
 Lower Bound to D-Efficiency = 0.9743

For $v = 16, b = 17$, the design obtained and the best available design are

D1: Best Available Design

(2, 5); (12, 1); (1, 8); (15, 12); (5, 3); (7, 4);
 (11, 14); (4, 13); (6, 15); (2, 11); (9, 10); (14, 9);
 (3, 6); (13, 16); (16, 2); (10, 1); (8, 7)

Lower Bound to A-Efficiency = 0.4351
 Lower Bound to D-Efficiency = 0.6620

D2: Design Obtained

(1, 9); (1, 10); (5, 1); (4, 3); (1, 7); (16, 1); (12, 1);
 (1, 4); (1, 6); (1, 8); (13, 1); (1, 11); (3, 1); (14, 1);
 (15, 1); (2, 5); (1, 2)

Lower Bound to A-Efficiency = 0.5199
 Lower Bound to D-Efficiency = 0.6145

Table 5.1. Comparison of designs obtained with best available designs

v	b	More efficient	Same	Less Efficient	Total
$3 \leq v \leq 5$	$b = v$	0	3	0	3
$6 \leq v \leq 10$	$v \leq b \leq v(v-1)/2$	3	105	2	110
$v = 11$	$v \leq b \leq v(v-1)/2$	2	41	2	45
$v = 12$	$v \leq b \leq v(v-1)/2$	3	43	9	55
$v = 13$	$v \leq b \leq v(v-1)/2$	2	44	20	66
$v = 14$	$v \leq b \leq v(v-1)/2$	3	47	28	78
$v = 15$	$v \leq b \leq v(v-1)/2$	7	52	32	91
$v = 16$	$v \leq b \leq v(v-1)/2$	10	50	45	105
$17 \leq v \leq 25$	$b = v$	0	9	0	9
Total		30	394	138	562

Remark 5.1. We compared the algorithm developed in the present investigation with that of Kerr and Churchill's (2001a). Kerr and Churchill quoted "There are 11,716,571 non-isomorphic connected graphs on 10 nodes. ... Obviously a naïve search of all possible designs becomes computationally infeasible for larger v ." One advantage of the proposed algorithm is that we can generate an efficient design in a shorter time.

Remark 5.2. For $9 \leq v = b \leq 20$, our designs have higher A-efficiencies than Nguyen and Williams's designs but have same A-efficiencies as that of Yang's designs (except for $v = 9, 10$ and 11 where our designs are less efficient than Yang's designs).

5.2 Comparison with BIB/PBIB(2) Designs

For block designs with number of treatments v , number of blocks $b = v(v-1)/2$ and block size 2, an unreduced BIB design is A- and D-optimal for inferring on a complete set of orthonormalized treatment contrasts. Computer aided search generated BIB designs for all $3 \leq v \leq 16$, $b = v(v-1)/2$ and $k = 2$. For the remaining parametric combinations in the range $4 \leq v \leq 16$, $v \leq b < v(v-1)/2$ and $17 \leq v = b \leq 25$, with block size $k = 2$, there does not exist a BIB design. PBIB(2) designs may be an answer for the parametric combinations for which a BIB design does not exist. Therefore, we compared PBIB(2) designs catalogued in Clatworthy (1973) with those of the best available block designs as well as with the designs obtained in the present investigation. There are 29 parametric combinations in the parametric range for which a PBIB(2) design is catalogued in Clatworthy (1973). We have calculated A-efficiencies of these PBIB(2) designs and compared with the best available block designs and the designs obtained using the algorithm. The results of comparisons are given in Table 5.2.

There do exist PBIB(2) designs for $v = 5, b = 10, k = 2$ [C2]; $v = 9, b = 36, k = 2$ [LS2] and $v = 10, b = 45, k = 2$ [T4] as well. For these parametric combinations unreduced BIB designs also exists. Therefore, these designs were not used for comparison purpose.

From Table 5.2, it is observed that for $(v, b) = (10, 30)$ and $(16, 48)$ the designs obtained have higher efficiencies than those of PBIB(2) designs as well as the best available block designs.

For $(v, b) = (9, 18), (10, 40), (13, 39)$ and $(15, 45)$, A-efficiencies of the designs obtained are same as that

Table 5.2. Efficiencies of PBIB(2) designs, best available block designs and the designs obtained

Sl. No.	v	b	PBIB (2) Design	A-Efficiency			Sl. No. in APP-END-IX Table 5.6
				PBIB(2) Design	Best Available Design	Design Obtained	
1	4	4	SR1	0.9000	0.9000	0.9000	2
2	5	5	C1	0.8000	0.8000	0.8000	3
3	6	9	SR6	0.9259	0.9259	0.9259	7
4	6	12	R18	0.9615	0.9615	0.9615	10
5	8	16	SR9	0.9423	0.9423	0.9423	37
6	8	24	R29	0.9800	0.9800	0.9800	45
7	9	18	LS1	0.8889	0.9087	0.9087	59
8	9	27	R34	0.9697	0.9697	0.9697	68
9	10	15	T2	0.8182	0.8182	0.8182	83
10	10	25	SR11	0.9529	0.9529	0.9529	93
11	10	30	T3	0.8182	0.9543	0.9570	98
12	10	40	R36	0.9783	0.9878	0.9878	108
13	12	36	SR13	0.9603	0.9603	0.9603	183
14	12	48	R38	0.9758	0.9758	0.9715	195
15	12	54	R39	0.9837	0.9837	0.9808	201
16	12	60	R40	0.9918	0.9918	0.9898	207
17	13	39	C10	0.9231	0.9441	0.9441	240
18	14	49	SR14	0.9657	0.9657	0.9657	315
19	15	45	T6	0.9175	0.9333	0.9333	388
20	15	60	T5	0.9409	0.9667	0.9651	403
21	15	75	R41	0.9800	0.9800	0.9777	418
22	16	40	M1	0.9000	0.9000	0.9000	473
23	16	48	LS3	0.8819	0.9251	0.9265	481
24	16	48	M2	0.8929	0.9251	0.9265	481
25	16	64	SR15	0.9698	0.9698	0.9698	497
26	16	72	LS4	0.9558	0.9693	0.9675	505
27	16	72	M5	0.9615	0.9693	0.9675	505
28	16	80	M3	0.9643	0.9752	0.9740	513
29	16	80	M4	0.9000	0.9752	0.9740	513

Bold faced efficiency in any row indicates the maximum efficiency for that parametric combination (when at least two A-efficiencies among the three designs differ) in the table. X #denotes the PBIB(2) design of type X at serial number # in Clatworthy (1973).

of best available designs and higher than those of PBIB(2) designs.

For $(v, b) = (12, 48), (12, 54), (12, 60)$ and $(15, 75)$, A-efficiencies of PBIB(2) designs are same as that of best available designs.

For $(v, b) = (15, 60), (16, 72)$ and $(16, 80)$, A-efficiencies of the best available designs are higher than those of PBIB(2) designs.

For the remaining cases all the three PBIB(2) designs, best available designs and the designs obtained have same lower bound to A-efficiency.

In nutshell, we can say that the PBIB(2) designs are at most as efficient as the best available designs/designs obtained in the present investigation.

6. ROBUSTNESS OF EFFICIENT BLOCK DESIGNS UNDER MIXED EFFECTS MODEL

Till now optimality aspects of designs for two-colour microarray experiments have been studied under fixed effects model. Indeed it is possible that the designs which are A-optimal/efficient under a fixed effects model may not be A-optimal/efficient under a mixed effects model. Hence, there is need to study how the designs that are A-efficient under fixed effects model perform under a mixed effects model considering array effects random. The lower bound to A-efficiency in a mixed effects model depends on $\rho = \sigma^2 / (\sigma^2 + k\sigma_\beta^2)$. ρ is generally unknown and so we need to search designs that are robust against the values of ρ in terms of A-efficiency. We, therefore, investigate the robustness of the designs under fixed effects model ($\rho = 0$) against different values of ρ in the range $0 \leq \rho \leq 0.9$ under mixed effects model. For this purpose, lower bounds to A-efficiencies of the efficient designs under fixed effects model are studied for $0 \leq \rho \leq 0.9$. Then percent coefficient of variation (CV) of lower bound to A-efficiencies for $0 \leq \rho \leq 0.9$ is also computed.

A design is said to be robust (strongly robust) if the CV of the A-efficiencies is smaller than 5% (1%). Lower bound to the A- and D-efficiencies of designs for microarrays under a mixed effects model in block design setup have been obtained for all the block designs (best available and designs obtained in the present investigation). A-efficient designs are generated for $\rho = 0$, i.e. under fixed effects model and CV of the

lower bound to A-efficiencies of the generated design for different values of $0 \leq \rho \leq 0.9$ is computed. The number of designs which are strongly robust, robust or not robust is given in Table 5.3.

Table 5.3. Robustness of designs obtained and best available designs

Design Obtained				
	Efficiency			Total
	More	Same	Less	
Strongly Robust	7	153	68	228
Robust	18	172	56	246
Not Robust	5	69	14	88
Total	30	394	138	562

Best Available Design				
	Efficiency			Total
	Less	Same	More	
Strongly Robust	5	153	70	228
Robust	16	172	52	239
Not Robust	9	69	17	95
Total	30	394	138	562

Among the 562 designs obtained, 228 designs are found to be strongly robust and 246 designs are found to be robust under linear mixed effects model. The remaining 88 designs which are not robust in the range $0 \leq \rho \leq 0.9$ are found to be robust in the range $0.3 \leq \rho \leq 0.9$.

Similarly, among 562 best available designs, 228 designs are found to be strongly robust and 239 designs are found to be robust under mixed effects model. The remaining 95 designs which are not robust in the range $0 \leq \rho \leq 0.9$, are found to be robust in the range $0.3 \leq \rho \leq 0.9$.

Out of 228 strongly robust designs, 226 parametric combinations were same for designs obtained and best available designs. For 2 parametric combinations $v = 10, b = 33, k = 2$ and $v = 15, b = 66, k = 2$, the designs obtained are strongly robust where as the best available designs are robust. For these parametric combinations designs obtained are also more efficient than the best available block designs and are given at serial numbers 3 and 20 in Table 5.6. For parametric combinations $v = 12, b = 45, k = 2$ and $v = 14, b = 59, k = 2$ the best available designs are strongly robust and the designs

obtained are robust. For these two parametric combinations, designs obtained are less efficient than the best available designs. Therefore, it is recommended that for these two parametric combinations, the designs available in the literature should be used. The block contents of the best available designs for these parametric combinations are D1 : $v = 12, b = 45, k = 2$: (11, 1); (7, 2); (5, 11); (5, 6); (9, 5); (11, 6); (2, 9); (7, 5); (8, 4); (8, 12); (7, 12); (12, 9); (3, 7); (1, 2); (6, 8); (5, 10); (5, 8); (10, 12); (1, 7); (9, 1); (6, 10); (7, 4); (3, 4); (9, 3); (1, 6); (9, 4); (3, 8); (2, 3); (4, 11); (6, 9); (4, 1); (2, 5); (1, 10); (10, 2); (12, 6); (11, 3); (4, 10); (10, 3); (4, 5); (3, 12); (12, 11); (6, 7); (8, 1); (8, 2) and (2, 11) and D2: $v = 14, b = 59, k = 2$: (1, 3); (9, 10); (10, 6); (7, 5); (3, 8); (3, 4); (2, 14); (3, 2); (2, 4); (7, 6); (11, 5); (13, 2); (3, 14); (1, 10); (5, 3); (3, 12); (6, 3); (4, 12); (13, 10); (9, 4); (13, 12); (10, 7); (9, 12); (2, 10); (1, 5); (1, 6); (7, 8); (5, 14); (11, 4); (12, 6); (5, 9); (11, 2); (1, 14); (12, 7); (4, 7); (11, 8); (6, 11); (5, 6); (12, 1); (9, 2); (7, 2); (14, 11); (12, 11); (14, 7); (4, 13); (8, 9); (6, 13); (8, 13); (2, 1); (13, 5); (14, 9); (8, 5); (4, 8); (4, 1); (10, 11); (6, 9); (14, 13); (8, 1) and (10, 3). Both these designs are obtained by Nguyen and Willimas (2005).

Among 30 more A-efficient designs obtained than the best available designs 7 designs are found to be strongly robust, 18 designs are found to be robust and remaining 5 designs are not robust under mixed effects model. For those 30 parametric combinations 5 designs are strongly robust, 16 are robust and 9 are not robust among the best available block designs. To study the not robust designs among the designs obtained and the best available block designs, it is found that, the 5 more A-efficient designs obtained which are not robust under mixed effects model are among the 9 best available block designs which are not robust under mixed effects model. Therefore, we can say that the more A-efficient designs obtained in the present investigation are also more robust under a mixed effects model.

The more efficient designs with their A- and D-efficiencies and A- and D-efficiencies of corresponding best available block designs are catalogued in Table 5.6 in APPENDIX. We also made a comparison of more efficient designs obtained and the best available designs using both the criteria viz. robustness and also CV(A-efficiencies). The results are shown under the columns 'Robustness' and 'CV(Eff)' in Table 5.6 in APPENDIX and are summarized in Table 5.4.

Table 5.4. More efficient designs: Robustness versus CV(A-Efficiencies)

	Strongly Robust	Robust	Not Robust	Total
less CV(A-eff)%	7	17	5	29
same CV(A-eff)%	0	0	0	0
more CV(A-eff)%	0	1	0	1
Total	7	18	5	30

Out of 30 designs which are more efficient 29 designs have less CV(A-efficiencies) and 1 design has more CV(A-efficiencies) than the best available block designs. In Table 5.6 (in APPENDIX), we also give lower bounds to A-efficiency of the designs obtained which are more efficient than the best available ones. We find that, out of 29 designs (with less CV) 21 designs have more A-efficiencies for smaller values of ρ 's and the A-efficiencies become same for higher values of ρ 's. The number of designs and the value of ρ at which the A-efficiencies become same are summarized as

A-Efficiencies become same at ρ value	No. of Designs
0.1	1
0.4	3
0.5	3
0.6	9
0.7	3
0.8	2
Total	21

The remaining 8 designs with parameters (v, b): (12, 13); (13, 17); (14, 15); (14, 18); (15, 16); (16, 17); (16, 18) and (16, 20) have more A-efficiencies at $\rho = 0.0$ and less A-efficiencies for all other values of ρ 's ($= 0.1$ to 0.9). Among these 8 designs which have more A-efficiencies at $\rho = 0.0$ and less A-efficiencies for all other values of ρ 's ($= 0.1$ to 0.9), for 4 parametric combinations (v, b): (14, 15); (15, 16); (16, 17) and (16, 18) the designs obtained are robust whereas the best available block designs are not robust and for the remaining 4 parametric combinations with parameters (v, b): (12, 13); (13, 17); (14, 18) and (16, 20) both the designs obtained and the best available block designs are not robust.

Among 394 designs with same A-efficiency, 153 designs are found to be strongly robust, 172 designs are found to be robust and remaining 69 designs are not robust for both the designs obtained and the best available block designs under linear mixed effects model. Among the 394 designs with same A-efficiency 393 designs have same A-efficiency for different values of $\rho = 0.0$ to 0.9 for both the designs obtained and the best available block designs and for $v = 15$ and $b = 20$, the A-efficiency is same for $\rho = 0.0$ and the A-efficiencies of the design obtained are less than the A-efficiencies of best available block designs for $\rho = 0.1, 0.2, \dots, 0.9$. Therefore, for $v = 15, b = 20$, the best available design is preferred over the design obtained although the A-efficiency of both the designs under fixed effects model is same.

Among 138 designs obtained with less A-efficiency 68 designs are found to be strongly robust, 56 designs are found to be robust and remaining 14 designs are not robust under mixed effects model whereas for those 138 parametric combinations 70 designs are strongly robust, 51 are robust and 17 are not robust among the best available block designs. Out of the 7 new designs obtained (Table 5.7 in APPENDIX) 3 designs are strongly robust and 4 designs are robust.

7. BLOCK DESIGNS FOR 3-COLOUR MICROARRAYS

In the earlier section we have exploited the algorithm for computer aided search of efficient block designs for 2-colour microarray experiments. Now a days three- and four-colour microarrays are also proposed where more than two (*i.e.* three or four or more) dyes may be used in a single microarray experiment (see e.g. Woo *et al.* 2005). The algorithm and Visual C++ code developed in the present investigation is general in nature and can be used for generation of efficient proper block designs for any v, b, k such that $2 \leq k < v$. For illustration, we give 4 examples of block designs for block size $k = 3$ in Table 5.5.

8. EFFICIENT BLOCK DESIGNS FOR A GIVEN VALUE OF ρ

In the earlier sections, to obtain efficient and robust block designs under a mixed effects model, we have adopted a two pronged strategy. First we obtain an efficient block design under a fixed effects model and then study the variation in A-efficiencies of this design

Table 5.5. Some block designs for 3-colour microarray experiments

v	b	k	A-Efficiency	D-Efficiency	CV(A-Eff)	CV(D-Eff)
6	4	3	0.9615	0.9801	1.2588	0.6475
Block Contents : (3, 5, 6); (2, 4, 5); (1, 3, 4); (6, 2, 1)						
6	6	3	0.9804	0.9903	0.6358	0.3124
Block Contents : (3, 1, 6); (6, 2, 1); (2, 5, 3); (4, 3, 2); (5, 6, 4); (1, 4, 5)						
6	8	3	0.9845	0.9922	0.5028	0.2520
Block Contents : (2, 3, 6); (6, 5, 3); (1, 3, 4); (5, 1, 6); (4, 6, 2); (4, 2, 5); (1, 2, 5); (3, 4, 1)						
7	7	3	1.0000	1.0000	0.0000	0.0000
Block Contents : (2, 7, 3); (4, 6, 7); (3, 1, 4); (1, 2, 6); (7, 5, 1); (5, 4, 2); (6, 3, 5)						

for different values of $0.0 \leq \rho \leq 0.9$. It may happen that a design which is optimal/efficient under mixed effects model *i.e.* for a particular value of ρ may have more A-efficiency than the design which is optimal/efficient under fixed effects model (*i.e.* for $\rho = 0.0$) at that particular value of ρ . For example, for $v = 9, b = 9$ and $k = 2$, the design obtained [D1: Mix(3)] and best available design [D2: Mix(4)] under fixed effects model have less lower bound to A-efficiency than the design D3 (loop design) at $\rho = 0.4$.

D1: Design obtained under fixed effects model	
Block Contents: (1, 5); (1, 8); (1, 7); (1, 9); (2, 3); (1, 4); (1, 6); (3, 1); (1, 2)	
A-efficiency ($\rho = 0.0$) = 0.5517	
A-efficiency ($\rho = 0.4$) = 0.6031	

D2: Best Available Design under fixed effects model	
Block Contents: (1, 5); (1, 8); (1, 7); (1, 9); (2, 3); (3, 4); (1, 6); (4, 1); (1, 2)	
A-efficiency ($\rho = 0.0$) = 0.5565	
A-efficiency ($\rho = 0.4$) = 0.6440	

D3: Loop Design	
Block Contents: (5, 8); (9, 1); (6, 5); (4, 3); (8, 4); (3, 2); (7, 9); (2, 7); (1, 6)	
A-efficiency ($\rho = 0.0$) = 0.5333	
A-efficiency ($\rho = 0.4$) = 0.9247	

Therefore, one may attempt to obtain an optimal/efficient design in the class $\mathbf{D}(v, b, k, \rho)$ for a particular value of ρ and to study the behaviour for different values of ρ . In other words, the problem is to obtain optimal/efficient proper block design for a given value of $\rho = \sigma^2 / (\sigma^2 + k\sigma_\beta^2)$. We are searching for a proper block design. However, while applying the exchange step of the algorithm, the search of weakest observation by deleting a treatment from a block one at a time, renders the design with two distinct block sizes viz. $k - 1$ and k . Therefore, for computation of trace $(\mathbf{C}_{n-1}^- \mathbf{P}\mathbf{P}')$, the \mathbf{C} matrix in (2.1a) should be used in place of \mathbf{C} -matrix given in (2.1c). The \mathbf{C} -matrix given in (2.1a) involves $\mathbf{W} = \text{diag}(w_1, \dots, w_b)$, a diagonal matrix of w_j , where $w_j = \sigma_\beta^2 / (\sigma^2 + k_j \sigma_\beta^2) \forall j = 1(1)b$. Therefore, we need to compute w_j values for a given ρ . The procedure of obtaining w_j values is described in the sequel.

Since, in the exchange step, after deletion of single observation there is one block of size $k - 1$ and $b - 1$ blocks are of size k . Therefore, w_j values are of two kinds, say w_{k-1} for the block with deleted observation and w_k for all other $(b - 1)$ blocks. Under a proper block design set up

$$\rho = \frac{\sigma^2}{\sigma^2 + k\sigma_\beta^2} = \frac{1}{1 + k\sigma_\beta^2/\sigma^2}$$

But when block sizes differ ρ values will depend on block size as σ_β^2/σ^2 is constant. From the above, $\sigma_\beta^2/\sigma^2 = (1 - \rho)/k\rho$. Substituting the value of σ_β^2/σ^2 in $w_j = \sigma_\beta^2 / (\sigma^2 + k_j \sigma_\beta^2)$ for computing w_{k-1} and w_k , we get

$$w_{k-1} = \frac{\sigma_\beta^2/\sigma^2}{1 + (k-1)\sigma_\beta^2/\sigma^2} = \frac{(1-\rho)/k\rho}{1 + (k-1)(1-\rho)/k\rho}$$

$$= \frac{(1-\rho)}{k\rho + (k-1)(1-\rho)} = \frac{(1-\rho)}{k - (1-\rho)} \quad (8.1)$$

$$w_k = \frac{\sigma_\beta^2/\sigma^2}{1 + k\sigma_\beta^2/\sigma^2} = \frac{(1-\rho)/k\rho}{1 + k(1-\rho)/k\rho}$$

$$= \frac{(1-\rho)}{k\rho + k(1-\rho)} = \frac{(1-\rho)}{k}$$

Therefore, in exchange step with $n - 1$ observations the \mathbf{W} -matrix becomes a $b \times b$ diagonal matrix of w_{k-1}

and w_k where w_{k-1} is placed in the q^{th} diagonal position (if one observation is deleted from q^{th} block) and w_k is placed in all other positions.

Now, these \mathbf{W} -matrices for proper and non-proper block designs can be used in the algorithm for obtaining optimal/efficient block designs in the class $\mathbf{D}(v, b, k, \rho)$ for a particular value of ρ and to study the behaviour of that design under a mixed effects model considering block/array effects as random.

In the present investigation, we are considering block designs with block size 2 i.e. we are searching block design in the class $\mathbf{D}(v, b, 2, \rho)$. Therefore, for this situation w_{k-1} and w_k values reduces to w_1 and w_2 . The value of w_1 and w_2 are computed for different values of $\rho = 0.0, 0.1, 0.2, \dots, 0.9$ using (2.5) and (2.6) and are given as

ρ	w_1	w_2
0.1	0.8182	0.4500
0.2	0.6667	0.4000
0.3	0.5385	0.3500
0.4	0.4286	0.3000
0.5	0.3333	0.2500
0.6	0.2500	0.2000
0.7	0.1765	0.1500
0.8	0.1111	0.1000
0.9	0.0526	0.0500

9. DISCUSSION

In the present investigation, two different approaches for obtaining efficient and robust designs for microarray experiments have been discussed. There may be another possibility of obtaining efficient designs using Bayesian approach. One may consider putting a Beta prior on the ratio of the variance components and then derive efficient designs after taking the expectation with respect to beta distribution. This approach requires a lot of derivations and computations and will be dealt with separately.

Further, in the present investigation, it has tacitly been assumed that the variability in gene expression is constant across all the genes. Depending upon the

underlying biology, the gene expressions may be heteroscedastic and depend upon the gene of interest. This is another important issue which needs attention. This amounts to obtaining efficient block designs under a heteroscedastic set up.

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APPENDIX

Table 5.6. More Efficient Block Designs than Best Available Block Designs for 2-colour Microarray Experiments in Parametric Range
 $6 \leq v \leq 16$, $v \leq b \leq v(v-1)/2$ and 3, 4, 5, $17 \leq v \leq 25$ and $b = v$

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness	lessCV %
1	9	25	A-Eff	0.9515	0.9628	0.9712	0.9775	0.9822	0.9856	0.9881	0.9898	0.9910	0.9916	1.3077	Robust	lessCV
	9	25	A-Eff	0.9480	0.9607	0.9699	0.9768	0.9818	0.9855	0.9881	0.9898	0.9910	0.9916	1.4205	Robust	
	9	25	D-Eff	0.9743	0.9805	0.9850	0.9883	0.9907	0.9925	0.9937	0.9946	0.9951	0.9953	0.6779		
	9	25	D-Eff	0.9607	0.9798	0.9846	0.9881	0.9906	0.9924	0.9937	0.9945	0.9951	0.9953	0.7145		
Design Obtained			: (3, 7); (4, 9); (5, 3); (6, 9); (8, 4); (8, 6); (5, 8); (7, 2); (6, 3); (6, 1); (4, 7); (5, 7); (2, 4); (3, 4); (2, 6); (1, 3); (1, 2); (9, 5); (7, 8); (8, 1); (7, 9); (4, 6); (9, 1); (2, 5); (1, 5).													
Best Available Design			: (7, 1); (6, 3); (2, 1); (4, 8); (1, 4); (7, 2); (8, 5); (3, 5); (9, 7); (2, 6); (8, 9); (9, 6); (5, 6); (6, 1); (2, 3); (8, 2); (3, 9); (1, 8); (9, 4); (4, 7); (4, 5); (1, 3); (5, 7); (5, 2); (3, 4).													
2	10	30	A-Eff	0.9570	0.9696	0.9788	0.9856	0.9905	0.9940	0.9965	0.9982	0.9993	0.9998	1.3846	Robust	lessCV
	10	30	A-Eff	0.9543	0.9679	0.9778	0.9850	0.9902	0.9939	0.9965	0.9982	0.9993	0.9998	1.4704	Robust	
	10	30	D-Eff	0.9774	0.9841	0.9890	0.9925	0.9951	0.9970	0.9982	0.9991	0.9996	0.9999	0.7233		
	10	30	D-Eff	0.9679	0.9835	0.9886	0.9923	0.9950	0.9969	0.9982	0.9991	0.9996	0.9999	0.7561		
Design Obtained			: (3, 4); (7, 8); (8, 2); (5, 8); (7, 9); (3, 7); (1, 3); (6, 10); (6, 7); (10, 9); (4, 5); (10, 8); (10, 3); (9, 1); (2, 4); (4, 9); (1, 2); (1, 5); (7, 2); (3, 6); (6, 1); (9, 3); (9, 5); (5, 7); (2, 6); (4, 6); (8, 1); (2, 10); (5, 10); (8, 4).													
Best Available Design			: (9, 1); (6, 10); (5, 3); (7, 1); (8, 4); (10, 9); (1, 5); (6, 2); (1, 2); (4, 6); (7, 10); (5, 10); (9, 6); (6, 7); (9, 8); (3, 6); (3, 4); (10, 3); (5, 4); (2, 9); (4, 9); (2, 7); (7, 8); (8, 5); (4, 7); (3, 2); (8, 3); (10, 1); (1, 8); (2, 5).													
3	10	33	A-Eff	0.9653	0.9733	0.9794	0.9839	0.9873	0.9898	0.9916	0.9929	0.9937	0.9942	0.9376	S-robust	lessCV
	10	33	A-Eff	0.9623	0.9715	0.9783	0.9834	0.9870	0.9897	0.9916	0.9929	0.9937	0.9942	1.0328	Robust	
	10	33	D-Eff	0.9815	0.9860	0.9893	0.9917	0.9934	0.9947	0.9956	0.9962	0.9966	0.9968	0.4919		
	10	33	D-Eff	0.9715	0.9853	0.9889	0.9915	0.9933	0.9947	0.9956	0.9962	0.9966	0.9968	0.5246		
Design Obtained			: (5, 10); (9, 2); (1, 2); (9, 10); (2, 3); (10, 3); (10, 4); (3, 7); (9, 7); (3, 6); (4, 6); (10, 2); (5, 9); (9, 1); (4, 7); (3, 5); (8, 6); (6, 1); (7, 1); (8, 3); (1, 5); (2, 4); (1, 3); (5, 8); (2, 8); (7, 8); (4, 5); (8, 9); (6, 9); (4, 8); (1, 4); (6, 10); (7, 10).													
Best Available Design			: (9, 2); (4, 10); (7, 5); (9, 8); (7, 10); (1, 5); (10, 9); (3, 4); (1, 6); (3, 6); (8, 7); (5, 3); (7, 4); (2, 8); (1, 10); (2, 1); (4, 9); (9, 1); (3, 8); (10, 3); (2, 3); (2, 7); (6, 2); (6, 5); (10, 6); (5, 4); (8, 6); (1, 7); (5, 9); (6, 4); (4, 2); (8, 5); (3, 1).													
4	11	24	A-Eff	0.8948	0.9220	0.9419	0.9565	0.9672	0.9750	0.9805	0.9843	0.9868	0.9881	3.0969	Robust	lessCV
	11	24	A-Eff	0.8922	0.9207	0.9412	0.9561	0.9670	0.9749	0.9805	0.9844	0.9868	0.9881	3.1788	Robust	
	11	24	D-Eff	0.9433	0.9583	0.9692	0.9770	0.9827	0.9868	0.9896	0.9915	0.9927	0.9934	1.6285		
	11	24	D-Eff	0.9207	0.9581	0.9690	0.9769	0.9826	0.9867	0.9896	0.9915	0.9927	0.9934	1.6393		
Design Obtained			: (1, 5); (8, 6); (5, 7); (6, 2); (5, 6); (7, 8); (8, 4); (2, 4); (9, 2); (6, 11); (9, 1); (3, 7); (11, 9); (2, 3); (11, 10); (4, 11); (10, 2); (10, 1); (1, 8); (8, 10); (1, 3); (7, 9); (3, 11); (4, 5).													
Best Available Design			: (10, 3); (6, 11); (4, 6); (3, 8); (3, 4); (4, 5); (9, 1); (5, 10); (1, 6); (1, 2); (11, 7); (5, 1); (1, 3); (6, 10); (2, 7); (11, 5); (8, 9); (9, 4); (8, 11); (7, 9); (2, 8); (4, 2); (10, 2); (7, 3).													

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
5	11	26	A-Eff	0.9116	0.9341	0.9506	0.9629	0.9719	0.9786	0.9833	0.9866	0.9887	0.9898	2.5822	Robust lessCV
	11	26	A-Eff	0.9105	0.9334	0.9502	0.9627	0.9718	0.9785	0.9833	0.9865	0.9886	0.9898	2.6170	Robust
	11	26	D-Eff	0.9528	0.9651	0.9741	0.9807	0.9855	0.9889	0.9914	0.9930	0.9941	0.9946	1.3580	
	11	26	D-Eff	0.9334	0.9648	0.9739	0.9806	0.9854	0.9889	0.9914	0.9930	0.9941	0.9946	1.3761	
	Design Obtained			: (9, 2); (6, 8); (11, 3); (3, 7); (11, 7); (1, 4); (6, 2); (7, 6); (5, 11); (1, 11); (8, 11); (10, 8); (9, 1); (2, 4); (10, 1); (2, 3); (7, 9); (5, 6); (4, 8); (9, 5); (4, 5); (3, 10); (1, 6); (8, 9); (5, 10); (7, 4).											
Best Available Design			: (3, 6); (6, 4); (5, 10); (1, 2); (10, 6); (7, 1); (2, 11); (5, 7); (2, 6); (10, 8); (7, 9); (8, 2); (1, 3); (2, 5); (9, 3); (8, 3); (11, 4); (8, 11); (6, 7); (11, 7); (9, 8); (4, 5); (4, 9); (4, 1); (3, 5); (1, 10).												
6	12	13	A-Eff	0.5387	0.6754	0.7581	0.8116	0.8473	0.8715	0.8878	0.8985	0.9052	0.9089	14.1960	Not lessCV robust
	12	13	A-Eff	0.5355	0.7009	0.8000	0.8636	0.9057	0.9340	0.9528	0.9649	0.9723	0.9762	15.9114	Not robust
	12	13	D-Eff	0.7540	0.8277	0.8717	0.8999	0.9187	0.9314	0.9399	0.9453	0.9486	0.9503	6.7863	
	12	13	D-Eff	0.7009	0.8492	0.8986	0.9302	0.9511	0.9651	0.9744	0.9805	0.9841	0.9859	7.3906	
	Design Obtained			: (11, 4); (12, 8); (1, 3); (10, 1); (4, 12); (7, 1); (5, 11); (2, 5); (6, 9); (8, 10); (9, 4); (1, 2); (3, 6).											
Best Available Design			: (5, 2); (7, 1); (1, 10); (9, 8); (12, 1); (4, 5); (6, 12); (11, 4); (3, 6); (10, 11); (8, 7); (2, 9); (2, 3).												
7	12	25	A-Eff	0.8799	0.9131	0.9373	0.9550	0.9680	0.9773	0.9839	0.9883	0.9911	0.9926	3.7473	Robust lessCV
	12	25	A-Eff	0.8781	0.9122	0.9369	0.9548	0.9679	0.9772	0.9839	0.9883	0.9911	0.9926	3.8040	Robust
	12	25	D-Eff	0.9350	0.9535	0.9668	0.9763	0.9831	0.9880	0.9914	0.9937	0.9951	0.9958	1.9767	
	12	25	D-Eff	0.9122	0.9533	0.9667	0.9762	0.9831	0.9880	0.9914	0.9937	0.9951	0.9958	1.9912	
	Design Obtained			: (4, 5); (1, 10); (2, 5); (10, 2); (5, 3); (11, 12); (11, 6); (2, 7); (10, 6); (6, 3); (12, 10); (5, 11); (1, 5); (9, 2); (2, 4); (3, 8); (6, 7); (3, 9); (8, 12); (8, 1); (4, 9); (7, 8); (9, 11); (9, 1); (7, 4).											
Best Available Design			: (7, 1); (5, 10); (11, 3); (7, 12); (9, 1); (1, 10); (9, 5); (8, 7); (11, 8); (4, 2); (8, 9); (1, 6); (10, 8); (5, 4); (4, 11); (12, 6); (3, 12); (6, 2); (12, 5); (10, 3); (3, 2); (6, 11); (1, 4); (2, 7); (2, 9).												
8	12	58	A-Eff	0.9863	0.9897	0.9921	0.9939	0.9951	0.9960	0.9967	0.9971	0.9973	0.9975	0.3572	S-robust lessCV
	12	58	A-Eff	0.9858	0.9894	0.9920	0.9938	0.9951	0.9960	0.9967	0.9971	0.9973	0.9975	0.3720	S-robust
	12	58	D-Eff	0.9931	0.9948	0.9960	0.9969	0.9975	0.9980	0.9983	0.9985	0.9986	0.9987	0.1757	
	12	58	D-Eff	0.9894	0.9947	0.9960	0.9969	0.9975	0.9980	0.9983	0.9985	0.9986	0.9987	0.1806	
	Design Obtained			: (8, 11); (6, 9); (1, 5); (4, 10); (10, 12); (2, 7); (6, 12); (8, 12); (3, 9); (5, 7); (4, 6); (8, 10); (9, 10); (12, 4); (4, 7); (3, 5); (2, 8); (7, 8); (9, 11); (9, 8); (7, 12); (1, 10); (11, 3); (5, 8); (11, 2); (1, 2); (8, 3); (4, 9); (1, 7); (1, 4); (4, 5); (6, 8); (5, 12); (5, 9); (10, 11); (2, 4); (7, 6); (8, 1); (2, 3); (5, 6); (11, 1); (6, 11); (10, 6); (12, 1); (7, 10); (9, 1); (10, 2); (12, 11); (12, 3); (10, 3); (3, 4); (7, 9); (12, 2); (2, 6); (3, 7); (9, 2); (11, 4); (11, 5).											
Best Available Design			: (3, 2); (12, 6); (7, 11); (7, 3); (3, 5); (8, 6); (2, 9); (9, 4); (7, 9); (1, 3); (5, 6); (12, 10); (11, 6); (4, 12); (11, 4); (1, 10); (5, 12); (5, 8); (1, 5); (3, 4); (2, 1); (2, 8); (11, 10); (11, 12); (7, 4); (7, 6); (3, 12); (9, 5); (9, 10); (4, 5); (10, 8); (5, 7); (6, 2); (4, 2); (9, 8); (1, 12); (9, 11); (4, 8); (5, 10); (6, 1); (12, 9); (2, 5); (1, 7); (6, 3); (4, 1); (8, 11); (6, 4); (3, 11); (2, 7); (12, 2); (11, 1); (10, 7); (6, 9); (10, 3); (8, 3); (8, 7); (8, 1); (10, 2).												

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness	%
9	13	17	A-Eff	0.6706	0.7587	0.8165	0.8556	0.8826	0.9012	0.9139	0.9224	0.9278	0.9308	9.5126	Not robust	lessCV
	13	17	A-Eff	0.6683	0.7676	0.8329	0.8772	0.9077	0.9286	0.9428	0.9522	0.9579	0.9610	10.4569	Not robust	
	13	17	D-Eff	0.8206	0.8691	0.9004	0.9214	0.9358	0.9456	0.9522	0.9565	0.9591	0.9605	4.7585		
	13	17	D-Eff	0.7676	0.8799	0.9141	0.9370	0.9526	0.9633	0.9705	0.9752	0.9780	0.9795	5.1080		
Design Obtained			: (7, 4); (3, 7); (9, 3); (8, 9); (13, 5); (2, 7); (9, 6); (4, 13); (1, 5); (6, 11); (7, 10); (11, 2); (13, 8); (1, 12); (10, 1); (5, 11); (12, 9).													
Best Available Design			: (12, 3); (3, 5); (8, 5); (7, 11); (6, 7); (13, 8); (8, 10); (6, 12); (1, 2); (1, 4); (7, 13); (5, 9); (2, 6); (4, 3); (10, 1); (9, 2); (11, 4).													
10	13	24	A-Eff	0.8323	0.8770	0.9094	0.9330	0.9500	0.9622	0.9707	0.9764	0.9800	0.9819	5.0825	Not robust	lessCV
	13	24	A-Eff	0.8296	0.8757	0.9088	0.9327	0.9499	0.9621	0.9707	0.9764	0.9800	0.9819	5.1694	Not robust	
	13	24	D-Eff	0.9098	0.9350	0.9528	0.9654	0.9743	0.9807	0.9850	0.9879	0.9897	0.9906	2.6502		
	13	24	D-Eff	0.8757	0.9347	0.9526	0.9653	0.9743	0.9806	0.9850	0.9879	0.9897	0.9906	2.6736		
Design Obtained			: (8, 9); (3, 4); (11, 3); (6, 2); (6, 10); (10, 8); (4, 10); (3, 12); (9, 2); (1, 6); (8, 12); (13, 1); (9, 13); (7, 11); (1, 7); (12, 1); (2, 5); (13, 4); (5, 8); (11, 9); (2, 3); (5, 7); (10, 11); (4, 5).													
Best Available Design			: (3, 1); (9, 10); (2, 3); (10, 2); (3, 7); (5, 13); (8, 4); (12, 7); (7, 9); (11, 2); (8, 13); (6, 5); (7, 11); (5, 12); (9, 8); (6, 8); (11, 6); (4, 1); (1, 9); (10, 5); (13, 3); (2, 4); (1, 6); (4, 12).													
11	14	15	A-Eff	0.5246	0.5417	0.5538	0.5627	0.5696	0.5750	0.5793	0.5828	0.5856	0.5879	3.4789	Robust	lessCV
	14	15	A-Eff	0.4819	0.6785	0.7897	0.8591	0.9044	0.9345	0.9543	0.9671	0.9748	0.9788	18.0032	Not robust	
	14	15	D-Eff	0.6286	0.6399	0.6476	0.6530	0.6567	0.6593	0.6611	0.6623	0.6630	0.6634	1.6807		
	14	15	D-Eff	0.6785	0.8392	0.8941	0.9283	0.9507	0.9656	0.9755	0.9818	0.9856	0.9876	8.2512		
Design Obtained			: (1, 9); (13, 1); (1, 7); (2, 10); (12, 1); (10, 1); (1, 6); (1, 2); (1, 5); (4, 1); (14, 1); (3, 4); (1, 8); (11, 1); (1, 3).													
Best Available Design			: (4, 7); (9, 1); (7, 14); (11, 10); (6, 11); (13, 12); (3, 13); (14, 8); (8, 1); (12, 9); (1, 6); (2, 3); (2, 4); (10, 5); (5, 2).													
12	14	18	A-Eff	0.6464	0.7467	0.8105	0.8529	0.8817	0.9014	0.9147	0.9235	0.9291	0.9321	10.4596	Not robust	lessCV
	14	18	A-Eff	0.6452	0.7548	0.8252	0.8723	0.9044	0.9262	0.9410	0.9506	0.9566	0.9597	11.2811	Not robust	
	14	18	D-Eff	0.8091	0.8632	0.8973	0.9199	0.9351	0.9455	0.9525	0.9570	0.9597	0.9611	5.1698		
	14	18	D-Eff	0.7548	0.8731	0.9099	0.9342	0.9507	0.9619	0.9694	0.9742	0.9771	0.9787	5.4852		
Design Obtained			: (6, 9); (12, 3); (9, 8); (1, 7); (10, 6); (14, 11); (8, 5); (6, 11); (7, 13); (11, 4); (10, 1); (3, 10); (12, 14); (2, 12); (7, 2); (4, 7); (5, 12); (13, 8).													
Best Available Design			: (12, 7); (1, 4); (1, 12); (3, 6); (7, 5); (4, 10); (11, 8); (3, 9); (9, 2); (13, 7); (14, 8); (4, 3); (5, 2); (10, 5); (8, 1); (2, 14); (6, 13); (6, 11).													

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
13	14	68	A-Eff	0.9776	0.9835	0.9878	0.9909	0.9933	0.9949	0.9961	0.9969	0.9974	0.9977	0.6454	S-robust lessCV
	14	68	A-Eff	0.9773	0.9833	0.9877	0.9909	0.9932	0.9949	0.9961	0.9969	0.9974	0.9977	0.6550	S-robust
	14	68	D-Eff	0.9882	0.9914	0.9937	0.9953	0.9965	0.9974	0.9980	0.9984	0.9986	0.9988	0.3383	
	14	68	D-Eff	0.9833	0.9913	0.9936	0.9953	0.9965	0.9974	0.9980	0.9984	0.9986	0.9988	0.3417	
Design Obtained			:	(12, 13); (6, 13); (9, 10); (8, 9); (14, 5); (11, 14); (10, 12); (8, 12); (2, 10); (6, 9); (2, 8); (4, 10); (2, 6); (5, 7); (2, 4); (4, 9); (9, 11); (7, 12); (3, 10); (7, 11); (7, 14); (13, 14); (11, 12); (6, 11); (9, 1); (9, 5); (12, 3); (3, 5); (12, 2); (14, 4); (9, 14); (13, 5); (11, 2); (8, 13); (6, 7); (1, 7); (5, 8); (13, 4); (4, 6); (14, 2); (1, 8); (2, 7); (7, 10); (5, 6); (3, 4); (4, 7); (1, 2); (14, 1); (10, 5); (1, 3); (12, 14); (5, 2); (6, 12); (12, 9); (10, 11); (14, 3); (8, 3); (4, 8); (13, 9); (10, 13); (1, 6); (3, 6); (11, 13); (13, 1); (11, 3); (8, 11); (10, 1); (7, 8).											
Best Available Design			:	(7, 9); (4, 13); (5, 7); (4, 2); (3, 13); (6, 10); (5, 13); (13, 9); (13, 10); (2, 12); (9, 1); (9, 11); (2, 14); (5, 4); (7, 3); (1, 5); (8, 10); (3, 11); (8, 4); (7, 2); (13, 14); (13, 6); (1, 3); (8, 14); (11, 4); (1, 8); (11, 6); (1, 2); (3, 14); (7, 8); (5, 12); (3, 4); (5, 14); (4, 6); (11, 8); (11, 10); (1, 6); (7, 12); (8, 6); (12, 1); (3, 2); (6, 7); (12, 11); (14, 7); (11, 5); (9, 4); (9, 2); (4, 1); (2, 10); (4, 7); (14, 11); (6, 9); (2, 8); (14, 9); (10, 1); (10, 9); (6, 3); (10, 5); (12, 13); (14, 1); (2, 5); (6, 5); (12, 8); (9, 12); (10, 3); (8, 13); (10, 7); (12, 3).											
14	15	16	A-Eff	0.5220	0.5379	0.5490	0.5573	0.5637	0.5687	0.5727	0.5759	0.5785	0.5807	3.2554	Robust lessCV
	15	16	A-Eff	0.4567	0.6695	0.7858	0.8575	0.9040	0.9347	0.9550	0.9680	0.9758	0.9799	18.9690	Not robust
	15	16	D-Eff	0.6211	0.6316	0.6388	0.6438	0.6473	0.6497	0.6514	0.6525	0.6531	0.6535	1.5882	
	15	16	D-Eff	0.6695	0.8353	0.8923	0.9276	0.9506	0.9659	0.9759	0.9824	0.9863	0.9883	8.6256	
Design Obtained			:	(1, 9); (4, 1); (1, 7); (5, 1); (1, 8); (3, 5); (11, 1); (1, 6); (15, 1); (1, 3); (12, 1); (14, 1); (1, 10); (13, 1); (2, 4); (1, 2).											
Best Available Design			:	(2, 3); (9, 15); (2, 6); (3, 4); (8, 9); (10, 2); (6, 8); (15, 1); (11, 10); (14, 12); (7, 11); (5, 13); (4, 14); (13, 7); (12, 1); (1, 5).											
15	15	31	A-Eff	0.8524	0.8958	0.9266	0.9487	0.9646	0.9758	0.9836	0.9888	0.9920	0.9937	4.7166	Robust lessCV
	15	31	A-Eff	0.8516	0.8952	0.9262	0.9485	0.9644	0.9757	0.9836	0.9888	0.9920	0.9937	4.7454	Robust
	15	31	D-Eff	0.9212	0.9450	0.9616	0.9733	0.9816	0.9874	0.9914	0.9940	0.9957	0.9965	2.4489	
	15	31	D-Eff	0.8952	0.9448	0.9615	0.9732	0.9815	0.9874	0.9914	0.9940	0.9957	0.9965	2.4581	
Design Obtained			:	(1, 5); (10, 2); (11, 4); (4, 6); (12, 15); (6, 13); (13, 14); (8, 12); (14, 7); (15, 2); (5, 12); (8, 3); (10, 4); (6, 7); (8, 11); (15, 1); (5, 9); (3, 10); (2, 6); (3, 13); (14, 10); (7, 8); (4, 5); (11, 15); (9, 13); (1, 3); (9, 8); (12, 14); (2, 9); (7, 1); (13, 11).											
Best Available Design			:	(1, 7); (7, 5); (5, 3); (6, 8); (13, 7); (1, 11); (3, 15); (6, 3); (7, 10); (5, 9); (11, 5); (11, 8); (3, 2); (15, 4); (2, 12); (15, 1); (9, 13); (2, 1); (14, 1); (12, 14); (4, 10); (14, 6); (8, 15); (2, 4); (10, 12); (9, 14); (4, 9); (8, 13); (13, 2); (10, 6); (12, 11).											
16	15	39	A-Eff	0.9024	0.9300	0.9499	0.9643	0.9747	0.9821	0.9874	0.9909	0.9931	0.9943	3.0232	Robust lessCV
	15	39	A-Eff	0.9021	0.9297	0.9496	0.9640	0.9745	0.9820	0.9873	0.9909	0.9931	0.9943	3.0356	Robust
	15	39	D-Eff	0.9476	0.9628	0.9735	0.9812	0.9867	0.9906	0.9934	0.9952	0.9963	0.9969	1.5929	
	15	39	D-Eff	0.9297	0.9625	0.9733	0.9811	0.9867	0.9906	0.9933	0.9952	0.9963	0.9969	1.6020	
Design Obtained			:	(11, 14); (3, 14); (8, 15); (9, 13); (5, 13); (1, 5); (7, 15); (10, 12); (8, 9); (2, 10); (15, 12); (6, 8); (5, 7); (13, 6); (1, 8); (11, 15); (13, 2); (14, 5); (3, 7); (9, 10); (3, 4); (12, 13); (14, 6); (12, 14); (4, 11); (10, 1); (9, 11); (6, 10); (14, 2); (4, 5); (12, 4); (7, 9); (6, 7); (2, 4); (4, 8); (1, 3); (11, 1); (15, 2); (13, 3).											
Best Available Design			:	(1, 14); (10, 1); (11, 12); (7, 4); (13, 5); (2, 7); (13, 9); (6, 9); (12, 10); (1, 3); (2, 14); (1, 6); (9, 10); (5, 1); (15, 5); (11, 5); (7, 11); (9, 11); (6, 15); (11, 3); (3, 8); (4, 14); (12, 8); (3, 2); (14, 12); (10, 2); (7, 1); (2, 6); (6, 12); (15, 10); (4, 3); (4, 15); (3, 13); (8, 15); (8, 13); (5, 2); (14, 13); (9, 4); (8, 7).											

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
17	15	42	A-Eff	0.9130	0.9364	0.9533	0.9656	0.9746	0.9810	0.9856	0.9887	0.9907	0.9917	2.5877	Robust lessCV
	15	42	A-Eff	0.9128	0.9364	0.9533	0.9656	0.9746	0.9810	0.9856	0.9887	0.9907	0.9917	2.5933	Robust
	15	42	D-Eff	0.9533	0.9662	0.9754	0.9820	0.9868	0.9902	0.9925	0.9941	0.9951	0.9956	1.3686	
	15	42	D-Eff	0.9364	0.9662	0.9754	0.9820	0.9868	0.9902	0.9925	0.9941	0.9951	0.9956	1.3662	
Design Obtained			:	(1, 9); (10, 3); (7, 13); (12, 15); (4, 9); (11, 2); (9, 7); (8, 13); (15, 7); (14, 1); (2, 15); (8, 14); (13, 2); (4, 10); (6, 11); (10, 5); (5, 6); (9, 8); (8, 3); (7, 14); (3, 6); (14, 5); (2, 5); (1, 6); (12, 10); (5, 9); (2, 3); (15, 8); (6, 15); (3, 7); (15, 4); (11, 12); (7, 11); (6, 13); (10, 1); (4, 11); (9, 12); (13, 10); (14, 4); (1, 2); (3, 4); (12, 14).											
Best Available Design			:	(15, 5); (2, 3); (5, 11); (5, 12); (7, 12); (2, 14); (6, 7); (6, 8); (4, 8); (7, 10); (1, 7); (10, 13); (13, 3); (2, 8); (3, 4); (1, 3); (13, 15); (12, 2); (4, 15); (14, 10); (8, 1); (14, 1); (10, 9); (3, 6); (11, 7); (4, 9); (5, 6); (9, 1); (10, 5); (15, 2); (8, 11); (6, 14); (14, 4); (9, 2); (12, 13); (8, 13); (12, 4); (7, 15); (11, 9); (3, 11); (9, 6); (1, 5).											
18	15	44	A-Eff	0.9247	0.9460	0.9612	0.9723	0.9803	0.9862	0.9903	0.9931	0.9949	0.9959	2.3206	Robust lessCV
	15	44	A-Eff	0.9234	0.9449	0.9604	0.9718	0.9800	0.9860	0.9902	0.9931	0.9949	0.9959	2.3693	Robust
	15	44	D-Eff	0.9596	0.9712	0.9795	0.9855	0.9898	0.9929	0.9950	0.9965	0.9974	0.9979	1.2347	
	15	44	D-Eff	0.9449	0.9706	0.9791	0.9853	0.9897	0.9928	0.9950	0.9965	0.9974	0.9979	1.2604	
Design Obtained			:	(7, 15); (11, 5); (13, 3); (8, 14); (5, 6); (14, 7); (9, 13); (6, 15); (2, 13); (9, 10); (5, 7); (1, 13); (4, 3); (11, 14); (2, 4); (4, 9); (3, 8); (13, 11); (15, 11); (6, 14); (4, 5); (1, 5); (1, 15); (14, 1); (13, 6); (12, 2); (14, 4); (10, 2); (10, 1); (3, 12); (6, 10); (7, 3); (12, 6); (5, 8); (8, 2); (15, 4); (9, 12); (7, 9); (15, 8); (10, 11); (2, 7); (8, 9); (12, 1); (11, 12).											
Best Available Design			:	(1, 9); (5, 12); (8, 9); (3, 7); (12, 10); (7, 6); (9, 4); (11, 1); (10, 6); (15, 11); (3, 11); (14, 8); (9, 10); (8, 12); (5, 6); (14, 1); (2, 1); (2, 13); (8, 2); (4, 11); (12, 4); (10, 15); (7, 2); (6, 13); (7, 15); (13, 9); (11, 8); (9, 5); (6, 4); (11, 5); (6, 8); (4, 14); (2, 5); (15, 13); (13, 12); (12, 7); (10, 3); (1, 7); (15, 14); (5, 3); (1, 10); (13, 3); (3, 14); (4, 2).											
19	15	65	A-Eff	0.9656	0.9746	0.9813	0.9862	0.9898	0.9924	0.9943	0.9955	0.9964	0.9968	1.0084	Robust lessCV
	15	65	A-Eff	0.9652	0.9744	0.9811	0.9861	0.9897	0.9924	0.9943	0.9955	0.9963	0.9968	1.0210	Robust
	15	65	D-Eff	0.9814	0.9865	0.9901	0.9928	0.9947	0.9961	0.9970	0.9977	0.9981	0.9983	0.5413	
	15	65	D-Eff	0.9744	0.9864	0.9901	0.9927	0.9947	0.9961	0.9970	0.9977	0.9981	0.9983	0.5468	
Design Obtained			:	(1, 5); (15, 6); (6, 10); (9, 13); (1, 14); (3, 9); (1, 9); (12, 13); (1, 11); (4, 14); (3, 14); (3, 12); (12, 8); (7, 8); (6, 7); (7, 9); (5, 6); (10, 3); (6, 9); (2, 12); (9, 14); (2, 8); (5, 7); (10, 2); (3, 5); (10, 12); (12, 4); (4, 10); (15, 1); (10, 1); (13, 10); (4, 15); (11, 6); (6, 8); (8, 1); (2, 15); (13, 4); (5, 13); (13, 14); (7, 10); (4, 5); (8, 3); (11, 4); (9, 2); (14, 7); (11, 7); (13, 15); (8, 11); (14, 15); (2, 5); (15, 11); (12, 1); (15, 3); (15, 7); (8, 4); (11, 2); (8, 13); (5, 10); (14, 2); (9, 4); (11, 3); (13, 11); (6, 12); (7, 12); (14, 6).											
Best Available Design			:	(5, 14); (4, 15); (14, 11); (15, 7); (1, 5); (11, 15); (11, 3); (13, 10); (6, 11); (2, 6); (1, 3); (3, 9); (6, 3); (3, 15); (5, 13); (14, 7); (8, 15); (7, 5); (3, 12); (13, 9); (10, 1); (4, 13); (14, 8); (8, 13); (1, 9); (1, 8); (8, 12); (2, 4); (9, 14); (15, 9); (10, 12); (4, 14); (6, 4); (9, 8); (10, 6); (10, 4); (2, 7); (12, 5); (7, 10); (1, 11); (4, 1); (3, 2); (6, 7); (7, 12); (5, 2); (7, 1); (10, 2); (15, 5); (5, 8); (12, 4); (12, 9); (15, 10); (5, 6); (9, 4); (11, 13); (13, 7); (12, 11); (2, 8); (13, 3); (6, 1); (9, 2); (14, 10); (3, 14); (11, 2); (8, 6).											
20	15	66	A-Eff	0.9668	0.9758	0.9824	0.9873	0.9908	0.9934	0.9952	0.9965	0.9972	0.9977	0.9942	S-robust lessCV
	15	66	A-Eff	0.9665	0.9757	0.9823	0.9872	0.9908	0.9934	0.9952	0.9965	0.9972	0.9977	1.0033	Robust
	15	66	D-Eff	0.9822	0.9872	0.9908	0.9934	0.9953	0.9966	0.9976	0.9982	0.9986	0.9988	0.5298	
	15	66	D-Eff	0.9757	0.9871	0.9907	0.9934	0.9953	0.9966	0.9975	0.9982	0.9986	0.9988	0.5342	
Design Obtained			:	(1, 8); (10, 4); (15, 10); (1, 2); (1, 3); (5, 12); (6, 9); (7, 9); (12, 14); (13, 15); (14, 10); (3, 13); (6, 14); (5, 7); (3, 10); (5, 13); (15, 1); (2, 12); (4, 9); (7, 8); (7, 15); (9, 12); (11, 1); (13, 2); (7, 11); (12, 8); (4, 5); (4, 7); (2, 6); (3, 12); (11, 6); (10, 11); (7, 3); (9, 13); (12, 11); (11, 13); (2, 5); (8, 11); (11, 2); (1, 5); (15, 3); (10, 2); (13, 4); (14, 3); (5, 14); (14, 1); (5, 6); (13, 8); (8, 10); (6, 8); (10, 5); (8, 14); (8, 9); (12, 4); (2, 7); (1, 4); (6, 15); (15, 2); (14, 13); (4, 6); (9, 1); (12, 15); (14, 7); (9, 10); (9, 15); (3, 6).											
Best Available Design			:	(2, 10); (3, 6); (6, 8); (9, 13); (3, 12); (7, 12); (9, 15); (6, 14); (4, 10); (1, 12); (10, 6); (15, 2); (7, 15); (13, 4); (10, 5); (1, 2); (3, 5); (14, 5); (7, 6); (8, 10); (11, 14); (11, 12); (14, 10); (6, 1); (5, 8); (4, 15); (11, 7); (5, 15); (15, 12); (12, 9); (4, 11); (11, 6); (13, 14); (3, 2); (15, 14); (5, 1); (13, 2); (4, 1); (1, 7); (7, 3); (2, 9); (9, 11); (9, 1); (8, 11); (6, 4); (12, 13); (12, 10); (8, 3); (4, 3); (10, 7); (14, 3); (14, 1); (7, 13); (12, 4); (5, 7); (9, 3); (5, 11); (6, 9); (8, 13); (15, 8); (2, 4); (1, 8); (8, 2); (13, 5); (10, 9); (2, 11).											

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
21	16	17	A-Eff	0.5199	0.5347	0.5451	0.5528	0.5587	0.5633	0.5671	0.5701	0.5725	0.5746	3.0583	Robust lessCV
	16	17	A-Eff	0.4351	0.6620	0.7825	0.8561	0.9036	0.9350	0.9556	0.9689	0.9768	0.9809	19.8038	Not robust
	16	17	D-Eff	0.6145	0.6244	0.6311	0.6357	0.6390	0.6413	0.6428	0.6438	0.6445	0.6448	1.5049	
	16	17	D-Eff	0.6620	0.8319	0.8908	0.9270	0.9505	0.9661	0.9763	0.9829	0.9869	0.9889	8.9573	
Design Obtained			: (1, 9); (1, 10); (5, 1); (4, 3); (1, 7); (16, 1); (12, 1); (1, 4); (1, 6); (1, 8); (13, 1); (1, 11); (3, 1); (14, 1); (15, 1); (2, 5); (1, 2).												
Best Available Design			: (2, 5); (12, 1); (1, 8); (15, 12); (5, 3); (7, 4); (11, 14); (4, 13); (6, 15); (2, 11); (9, 10); (14, 9); (3, 6); (13, 16); (16, 2); (10, 1); (8, 7).												
22	16	18	A-Eff	0.5181	0.5384	0.5522	0.5622	0.5696	0.5752	0.5795	0.5829	0.5856	0.5877	3.8139	Robust lessCV
	16	18	A-Eff	0.5102	0.6909	0.7930	0.8570	0.8990	0.9270	0.9455	0.9575	0.9647	0.9685	16.6229	Not robust
	16	18	D-Eff	0.6244	0.6381	0.6472	0.6535	0.6578	0.6608	0.6628	0.6642	0.6650	0.6654	1.9730	
	16	18	D-Eff	0.6909	0.8426	0.8939	0.9261	0.9473	0.9613	0.9707	0.9767	0.9803	0.9821	7.7211	
Design Obtained			: (5, 1); (16, 1); (1, 8); (3, 5); (14, 1); (13, 1); (1, 9); (1, 3); (1, 7); (6, 10); (1, 6); (15, 1); (10, 1); (4, 13); (1, 4); (1, 2); (1, 11); (12, 1).												
Best Available Design			: (13, 7); (1, 8); (7, 2); (12, 9); (2, 12); (11, 16); (3, 6); (4, 11); (8, 5); (15, 2); (5, 4); (9, 1); (3, 14); (16, 3); (4, 13); (6, 15); (10, 1); (14, 10).												
23	16	20	A-Eff	0.6034	0.7305	0.8077	0.8576	0.8908	0.9131	0.9281	0.9378	0.9438	0.9470	12.4868	Not robust lessCV
	16	20	A-Eff	0.6032	0.7340	0.8139	0.8658	0.9004	0.9237	0.9393	0.9494	0.9556	0.9589	12.8140	Not robust
	16	20	D-Eff	0.7917	0.8581	0.8982	0.9242	0.9415	0.9531	0.9608	0.9658	0.9688	0.9704	6.0239	
	16	20	D-Eff	0.7340	0.8624	0.9037	0.9304	0.9482	0.9602	0.9682	0.9733	0.9764	0.9780	6.1545	
Design Obtained			: (3, 4); (14, 3); (1, 13); (9, 15); (10, 15); (12, 2); (4, 5); (13, 14); (5, 8); (6, 12); (8, 6); (2, 11); (1, 7); (3, 10); (2, 16); (16, 3); (11, 1); (7, 5); (13, 9); (15, 6)												
Best Available Design			: (1, 9); (15, 3); (13, 4); (5, 11); (7, 14); (3, 7); (3, 12); (11, 2); (8, 16); (8, 15); (10, 6); (9, 6); (14, 5); (2, 1); (16, 1); (4, 8); (7, 10); (12, 2); (4, 5); (6, 13).												
24	16	35	A-Eff	0.8553	0.8959	0.9248	0.9455	0.9604	0.9710	0.9783	0.9832	0.9863	0.9879	4.4408	Robust moreCV
	16	35	A-Eff	0.8552	0.8960	0.9249	0.9456	0.9605	0.9710	0.9783	0.9832	0.9863	0.9879	4.4405	Robust
	16	35	D-Eff	0.9227	0.9450	0.9606	0.9716	0.9794	0.9849	0.9887	0.9911	0.9927	0.9935	2.3041	
	16	35	D-Eff	0.8960	0.9451	0.9607	0.9717	0.9795	0.9849	0.9887	0.9911	0.9927	0.9935	2.3031	
Design Obtained			: (11, 5); (13, 2); (1, 7); (7, 10); (8, 13); (15, 4); (16, 15); (15, 5); (12, 3); (1, 6); (4, 10); (14, 16); (9, 12); (14, 2); (5, 7); (9, 14); (2, 4); (4, 9); (6, 11); (9, 8); (5, 14); (3, 8); (10, 16); (12, 15); (3, 10); (7, 9); (13, 15); (16, 1); (10, 11); (2, 6); (11, 8); (6, 12); (8, 1); (7, 13); (14, 3).												
Best Available Design			: (13, 5); (15, 2); (15, 4); (9, 11); (1, 16); (5, 7); (2, 16); (3, 13); (5, 12); (7, 6); (5, 14); (16, 5); (13, 1); (4, 8); (2, 8); (10, 1); (3, 12); (9, 14); (12, 6); (14, 10); (2, 3); (10, 3); (16, 11); (4, 7); (8, 13); (14, 15); (1, 15); (6, 2); (7, 10); (12, 4); (8, 9); (6, 9); (11, 4); (11, 3); (6, 1).												
25	16	47	A-Eff	0.9185	0.9418	0.9586	0.9707	0.9794	0.9857	0.9902	0.9932	0.9951	0.9961	2.5347	Robust lessCV
	16	47	A-Eff	0.9179	0.9412	0.9581	0.9704	0.9792	0.9856	0.9901	0.9931	0.9950	0.9961	2.5584	Robust
	16	47	D-Eff	0.9564	0.9691	0.9782	0.9847	0.9894	0.9927	0.9950	0.9965	0.9975	0.9980	1.3403	
	16	47	D-Eff	0.9412	0.9688	0.9780	0.9846	0.9893	0.9926	0.9950	0.9965	0.9975	0.9980	1.3568	
Design Obtained			: (3, 7); (16, 2); (3, 4); (4, 16); (11, 6); (8, 10); (11, 3); (7, 14); (6, 9); (1, 12); (1, 10); (12, 8); (10, 15); (13, 15); (14, 2); (12, 7); (2, 12); (5, 8); (4, 6); (1, 13); (6, 14); (10, 16); (14, 8); (14, 1); (15, 11); (4, 12); (8, 13); (16, 11); (15, 5); (3, 5); (10, 3); (15, 14); (7, 16); (13, 4); (6, 10); (16, 5); (8, 11); (13, 2); (5, 9); (2, 3); (7, 13); (9, 7); (2, 9); (9, 1); (5, 6); (12, 15); (11, 1).												
Best Available Design			: (15, 5); (7, 9); (2, 8); (5, 3); (3, 8); (11, 4); (11, 14); (6, 11); (4, 1); (1, 16); (9, 5); (4, 2); (9, 11); (7, 4); (13, 8); (13, 4); (1, 14); (14, 3); (6, 10); (5, 14); (8, 9); (1, 6); (13, 16); (14, 2); (3, 6); (5, 16); (3, 7); (8, 15); (8, 1); (14, 10); (12, 1); (11, 15); (15, 10); (9, 12); (2, 12); (12, 3); (16, 7); (10, 13); (12, 13); (6, 13); (7, 2); (2, 6); (4, 5); (10, 9); (16, 11); (10, 7); (15, 12).												

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
26	16	48	A-Eff	0.9265	0.9485	0.9643	0.9757	0.9839	0.9899	0.9941	0.9970	0.9988	0.9997	2.3805	Robust lessCV
	16	48	A-Eff	0.9251	0.9476	0.9637	0.9753	0.9838	0.9898	0.9941	0.9969	0.9988	0.9997	2.4273	Robust
	16	48	D-Eff	0.9603	0.9724	0.9810	0.9871	0.9916	0.9948	0.9970	0.9984	0.9994	0.9999	1.2720	
	16	48	D-Eff	0.9476	0.9720	0.9807	0.9870	0.9915	0.9947	0.9970	0.9984	0.9994	0.9999	1.2919	
Design Obtained			:	(2, 7); (5, 10); (9, 16); (1, 14); (2, 13); (15, 2); (16, 3); (6, 14); (12, 6); (15, 1); (8, 11); (10, 15); (8, 13); (8, 9); (4, 5); (4, 6); (9, 4); (15, 3); (10, 16); (1, 7); (7, 8); (6, 8); (13, 3); (3, 5); (5, 12); (12, 9); (14, 5); (11, 16); (11, 15); (3, 7); (11, 14); (7, 12); (2, 4); (16, 1); (10, 13); (14, 9); (12, 11); (6, 10); (5, 8); (16, 2); (13, 1); (9, 15); (3, 6); (14, 2); (13, 12); (4, 11); (7, 10); (1, 4).											
Best Available Design			:	(13, 2); (5, 15); (5, 3); (1, 13); (7, 14); (9, 3); (1, 7); (11, 10); (14, 12); (2, 10); (10, 4); (15, 6); (5, 8); (3, 2); (6, 4); (1, 12); (9, 6); (11, 14); (4, 12); (3, 1); (2, 7); (15, 10); (13, 15); (14, 5); (7, 8); (6, 5); (6, 11); (12, 15); (13, 14); (15, 7); (10, 9); (8, 11); (7, 16); (16, 11); (4, 16); (4, 13); (11, 3); (14, 9); (12, 8); (3, 4); (16, 5); (8, 9); (2, 6); (8, 13); (12, 2); (10, 1); (16, 1); (9, 16).											
27	16	50	A-Eff	0.9275	0.9476	0.9622	0.9728	0.9805	0.9861	0.9900	0.9927	0.9944	0.9953	2.2133	Robust lessCV
	16	50	A-Eff	0.9271	0.9474	0.9620	0.9727	0.9804	0.9860	0.9900	0.9927	0.9944	0.9953	2.2247	Robust
	16	50	D-Eff	0.9609	0.9720	0.9799	0.9856	0.9897	0.9927	0.9947	0.9961	0.9970	0.9974	1.1786	
	16	50	D-Eff	0.9474	0.9718	0.9798	0.9856	0.9897	0.9927	0.9947	0.9961	0.9970	0.9974	1.1845	
Design Obtained			:	(1, 6); (6, 7); (7, 15); (7, 8); (9, 11); (10, 12); (13, 11); (4, 12); (6, 13); (10, 9); (5, 14); (8, 13); (3, 14); (15, 10); (5, 13); (4, 6); (12, 16); (4, 15); (11, 14); (14, 7); (2, 7); (14, 16); (1, 8); (7, 9); (3, 12); (8, 16); (8, 3); (16, 6); (12, 7); (4, 8); (2, 4); (13, 2); (1, 2); (12, 5); (2, 3); (14, 4); (10, 1); (13, 10); (15, 2); (16, 9); (15, 5); (11, 1); (9, 4); (14, 10); (6, 3); (15, 16); (3, 11); (11, 15); (9, 5); (5, 1).											
Best Available Design			:	(11, 15); (2, 5); (15, 9); (12, 3); (1, 12); (7, 2); (2, 11); (9, 16); (3, 2); (9, 8); (5, 9); (11, 6); (5, 10); (8, 14); (5, 12); (7, 16); (11, 4); (3, 16); (8, 11); (16, 11); (6, 3); (1, 6); (3, 8); (12, 7); (2, 13); (13, 15); (2, 1); (15, 12); (10, 4); (6, 5); (9, 1); (13, 6); (7, 8); (1, 10); (15, 10); (6, 7); (3, 14); (13, 4); (14, 1); (8, 13); (16, 1); (12, 4); (10, 7); (14, 15); (4, 14); (16, 13); (4, 2); (10, 3); (4, 9); (14, 5).											
28	16	73	A-Eff	0.9691	0.9776	0.9839	0.9886	0.9920	0.9945	0.9963	0.9975	0.9982	0.9987	0.9527	S-robust lessCV
	16	73	A-Eff	0.9680	0.9770	0.9835	0.9883	0.9919	0.9944	0.9962	0.9975	0.9982	0.9987	0.9873	S-robust
	16	73	D-Eff	0.9831	0.9879	0.9914	0.9939	0.9958	0.9971	0.9980	0.9987	0.9991	0.9993	0.5191	
	16	73	D-Eff	0.9770	0.9876	0.9912	0.9938	0.9957	0.9971	0.9980	0.9987	0.9991	0.9993	0.5319	
Design Obtained			:	(11, 14); (5, 12); (11, 2); (4, 2); (14, 10); (7, 16); (2, 13); (4, 9); (8, 12); (8, 15); (14, 4); (12, 15); (15, 2); (2, 8); (13, 15); (14, 8); (4, 12); (5, 2); (5, 14); (13, 10); (7, 14); (1, 12); (2, 7); (3, 14); (16, 8); (1, 11); (6, 11); (7, 15); (3, 10); (3, 15); (14, 13); (16, 13); (13, 9); (16, 3); (9, 5); (10, 4); (8, 1); (8, 6); (6, 4); (11, 16); (16, 5); (5, 1); (9, 8); (10, 9); (9, 16); (9, 7); (16, 4); (15, 5); (13, 1); (9, 11); (12, 13); (4, 1); (7, 6); (10, 8); (1, 9); (12, 3); (1, 3); (12, 11); (3, 2); (10, 7); (10, 5); (15, 6); (2, 14); (6, 3); (11, 10); (3, 9); (7, 12); (15, 4); (15, 11); (13, 6); (1, 7); (6, 16); (5, 6).											
Best Available Design			:	(9, 14); (7, 4); (5, 8); (11, 16); (16, 3); (11, 12); (5, 10); (3, 6); (9, 16); (7, 15); (9, 8); (8, 6); (11, 8); (13, 10); (1, 13); (9, 2); (1, 4); (2, 14); (11, 14); (5, 15); (15, 12); (9, 6); (1, 10); (3, 15); (3, 14); (7, 16); (5, 12); (16, 2); (1, 15); (10, 11); (13, 4); (10, 3); (10, 9); (6, 5); (6, 4); (16, 1); (12, 9); (3, 8); (4, 2); (4, 5); (7, 12); (5, 16); (16, 13); (3, 2); (8, 7); (12, 13); (16, 12); (14, 13); (6, 11); (8, 1); (1, 14); (12, 1); (4, 11); (12, 3); (15, 9); (4, 3); (15, 10); (4, 9); (10, 7); (2, 1); (8, 13); (13, 6); (15, 11); (7, 2); (14, 7); (2, 10); (6, 1); (2, 11); (14, 8); (2, 5); (13, 15); (14, 5); (6, 7).											
29	16	75	A-Eff	0.9685	0.9769	0.9830	0.9876	0.9909	0.9933	0.9950	0.9962	0.9969	0.9973	0.9292	S-robust lessCV
	16	75	A-Eff	0.9680	0.9766	0.9829	0.9875	0.9908	0.9933	0.9950	0.9961	0.9969	0.9973	0.9434	S-robust
	16	75	D-Eff	0.9830	0.9876	0.9910	0.9935	0.9952	0.9965	0.9974	0.9980	0.9984	0.9985	0.4989	
	16	75	D-Eff	0.9766	0.9876	0.9910	0.9934	0.9952	0.9965	0.9974	0.9980	0.9983	0.9985	0.5035	
Design Obtained			:	(11, 15); (2, 4); (6, 15); (10, 14); (14, 12); (5, 15); (6, 7); (7, 16); (4, 7); (11, 13); (14, 16); (13, 12); (3, 9); (5, 14); (1, 5); (3, 7); (2, 5); (5, 7); (1, 11); (2, 16); (1, 13); (2, 10); (5, 13); (5, 9); (9, 11); (3, 14); (14, 4); (9, 16); (16, 13); (8, 16); (15, 4); (14, 11); (1, 14); (6, 3); (15, 10); (7, 10); (9, 4); (1, 4); (10, 8); (8, 3); (8, 5); (6, 10); (12, 1); (8, 2); (2, 11); (13, 3); (4, 6); (11, 8); (3, 2); (3, 1); (16, 15); (13, 2); (7, 12); (4, 8); (16, 11); (12, 8); (9, 1); (10, 9); (10, 1); (15, 2); (14, 8); (6, 5); (7, 1); (13, 10); (15, 3); (11, 7); (9, 15); (8, 6); (15, 12); (4, 13); (16, 6); (11, 6); (12, 9); (12, 6); (12, 2).											
Best Available Design			:	(13, 6); (16, 6); (9, 1); (7, 10); (1, 12); (7, 14); (5, 7); (15, 6); (5, 8); (7, 4); (10, 3); (1, 10); (11, 4); (16, 10); (16, 12); (13, 2); (13, 4); (11, 8); (3, 4); (11, 1); (3, 13); (7, 2); (4, 16); (15, 2); (13, 8); (3, 15); (3, 8); (4, 6); (1, 7); (5, 4); (11, 10); (10, 13); (9, 10); (5, 16); (4, 2); (9, 12); (1, 6); (2, 9); (6, 5); (2, 11); (8, 1); (11, 12); (5, 14); (3, 5); (1, 2); (4, 9); (14, 11); (4, 15); (16, 11); (12, 7); (12, 15); (14, 1); (2, 3); (12, 3); (14, 3); (6, 7); (8, 15); (14, 13); (10, 5); (9, 13); (6, 3); (8, 16); (16, 14); (2, 16); (10, 15); (15, 14); (2, 5); (6, 11); (8, 9); (15, 1); (12, 13); (12, 5); (14, 9); (6, 9); (8, 7).											

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robust-CV(A-Eff) ness %
30	16	102	A-Eff	0.9888	0.9918	0.9940	0.9956	0.9967	0.9975	0.9980	0.9984	0.9986	0.9988	0.3169	S-robust lessCV
	16	102	A-Eff	0.9885	0.9917	0.9939	0.9955	0.9967	0.9975	0.9980	0.9984	0.9986	0.9988	0.3268	S-robust
	16	102	D-Eff	0.9943	0.9958	0.9969	0.9977	0.9983	0.9987	0.9990	0.9992	0.9993	0.9994	0.1623	
	16	102	D-Eff	0.9917	0.9958	0.9969	0.9977	0.9983	0.9987	0.9990	0.9992	0.9993	0.9994	0.1656	
Design Obtained			:	(5, 16); (9, 14); (7, 12); (2, 6); (6, 14); (7, 10); (1, 8); (11, 13); (5, 8); (6, 12); (7, 13); (2, 8); (12, 13); (5, 11); (3, 13); (4, 11); (3, 6); (5, 7); (3, 9); (10, 16); (9, 10); (15, 12); (4, 8); (16, 4); (6, 15); (4, 10); (8, 10); (15, 9); (14, 12); (3, 8); (2, 10); (12, 9); (13, 9); (5, 10); (6, 7); (1, 5); (1, 6); (16, 15); (8, 16); (13, 6); (4, 12); (11, 6); (11, 9); (2, 7); (11, 3); (7, 15); (2, 13); (12, 10); (7, 14); (2, 4); (14, 16); (15, 11); (16, 11); (13, 16); (9, 4); (14, 5); (10, 13); (8, 14); (12, 3); (6, 5); (5, 4); (10, 6); (5, 3); (16, 7); (1, 16); (7, 4); (6, 4); (1, 11); (1, 7); (15, 2); (9, 5); (10, 11); (14, 15); (11, 2); (12, 1); (11, 12); (13, 5); (11, 14); (16, 2); (9, 2); (8, 6); (8, 9); (10, 1); (8, 12); (14, 3); (4, 15); (16, 3); (9, 7); (13, 8); (7, 3); (3, 1); (15, 5); (15, 8); (9, 1); (4, 3); (13, 15); (3, 2); (12, 16); (10, 14); (15, 1); (14, 2); (2, 1).											
Best Available Design			:	(3, 15); (14, 6); (11, 4); (15, 7); (10, 8); (13, 10); (3, 11); (13, 11); (7, 13); (13, 4); (15, 4); (5, 13); (7, 16); (5, 10); (2, 13); (5, 7); (3, 12); (3, 2); (5, 2); (12, 14); (11, 5); (9, 14); (3, 14); (11, 2); (4, 10); (13, 8); (13, 16); (5, 12); (10, 3); (1, 6); (1, 13); (2, 14); (1, 5); (15, 2); (11, 14); (2, 6); (1, 4); (1, 3); (16, 12); (15, 10); (11, 9); (4, 6); (10, 11); (3, 8); (8, 12); (11, 12); (12, 1); (7, 11); (7, 4); (14, 8); (12, 10); (2, 16); (9, 1); (7, 8); (9, 16); (11, 6); (9, 15); (4, 2); (15, 12); (4, 8); (12, 9); (1, 14); (1, 7); (15, 6); (2, 10); (10, 7); (12, 13); (4, 9); (7, 3); (2, 9); (12, 4); (8, 1); (6, 7); (16, 1); (9, 5); (10, 1); (10, 9); (13, 6); (5, 15); (16, 11); (4, 5); (8, 16); (8, 2); (6, 10); (3, 5); (6, 16); (6, 9); (2, 1); (8, 9); (9, 7); (14, 15); (14, 5); (8, 11); (14, 7); (4, 3); (16, 3); (14, 13); (8, 15); (16, 15); (6, 3); (6, 12); (16, 5).											

Bold Faced indicates for the Designs obtained; Best Available Designs; are given below the Designs Obtained for each parametric combination

S-robust indicates that percentage CV(A-efficiency) of the design is less than 1%; Robust indicates that percentage CV(A-efficiency) of the design is less than 5%

Not robust indicates that percentage CV(A-efficiency) of the design is more than 5%

moreCV (lessCV) indicates that percentage CV(A-efficiency) of the design obtained in the present investigation is more (less)than the best available design

Table 5.7. Seven New Block Designs for 2-colour Microarray Experiments not Catalogued in Literature

Sl. No.	v	b	Eff	$\rho = 0.0$	$\rho = 0.1$	$\rho = 0.2$	$\rho = 0.3$	$\rho = 0.4$	$\rho = 0.5$	$\rho = 0.6$	$\rho = 0.7$	$\rho = 0.8$	$\rho = 0.9$	CV(Eff)	Robustness	
1	4	5	A-Eff	0.9000	0.9141	0.9252	0.9341	0.9411	0.9466	0.9509	0.9543	0.9568	0.9587	1.9927	Robust	
			D-Eff	0.9524	0.9580	0.9623	0.9656	0.9681	0.9699	0.9712	0.9722	0.9727	0.9731	0.6848		
Block Contents: (3, 4); (1, 3); (4, 1); (2, 4); (1, 2).																
*2	4	6	A-Eff	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	0.0000	S-robust
			D-Eff	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	0.0000	
Block Contents: (3, 4); (2, 3); (1, 2); (1, 3); (4, 2); (4, 1).																
3	5	6	A-Eff	0.8696	0.8908	0.9080	0.9219	0.9331	0.9419	0.9488	0.9539	0.9577	0.9601	0.9601	3.1342	Robust
			D-Eff	0.9277	0.9401	0.9497	0.9572	0.9629	0.9673	0.9704	0.9727	0.9741	0.9749	1.5819		
Block Contents: (3, 5); (4, 1); (3, 4); (1, 2); (2, 3); (5, 1).																
4	5	7	A-Eff	0.8905	0.9125	0.9294	0.9423	0.9522	0.9596	0.9651	0.9690	0.9717	0.9733	2.7975	Robust	
			D-Eff	0.9456	0.9565	0.9648	0.9710	0.9756	0.9790	0.9815	0.9832	0.9842	0.9848	1.2900		
Block Contents: (1, 5); (5, 2); (3, 5); (4, 1); (2, 3); (2, 4); (1, 3).																
5	5	8	A-Eff	0.9375	0.9504	0.9604	0.9681	0.9739	0.9783	0.9816	0.9839	0.9855	0.9864	1.6138	Robust	
			D-Eff	0.9682	0.9746	0.9794	0.9831	0.9858	0.9878	0.9892	0.9902	0.9908	0.9912	0.7472		
Block Contents: (4, 5); (3, 4); (2, 3); (1, 2); (1, 3); (4, 1); (2, 5); (5, 1).																
6	5	9	A-Eff	0.9524	0.9595	0.9650	0.9692	0.9725	0.9749	0.9768	0.9782	0.9792	0.9799	0.9019	S-robust	
			D-Eff	0.9779	0.9807	0.9829	0.9844	0.9856	0.9865	0.9871	0.9875	0.9878	0.9879	0.3246		
Block Contents: (4, 5); (5, 3); (3, 2); (1, 3); (4, 1); (2, 5); (2, 4); (5, 1); (1, 2).																
*7	5	10	A-Eff	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	0.0000	S-robust
			D-Eff	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000	0.0000	
Block Contents: (2, 4); (4, 1); (4, 5); (5, 2); (5, 1); (2, 3); (3, 4); (3, 5); (1, 3); (1, 2).																

The designs marked with aestrik (*) are balanced incomplete block (BIB) designs.