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# Constant Block Sum PBIB Designs based on Tetrahedral and Cubical Association Schemes

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## ABSTRACT

**Background:** In biomedical studies, particularly those involving animals, the carryover effects from previous experiments necessitate a repeated measures approach. In this context, constant block-sum designs are particularly relevant, especially in situations where treatments are quantitative and there's a desire for all units to be exposed to the same cumulative dose at the experiment's conclusion.

**Methods:** This article discusses two distinct methods for constructing constant block-sum PBIB designs, supplemented with illustrative examples.

**Result:** The most advantage of these designs is that if we wish to do experiment in subsequence form, the set of experimental units used, as homogeneous and thus can reuse them in later subsequent experiments.

**Key words:** Association scheme, Constant block-sum, Incomplete block designs- BIBD and PBIB.

## INTRODUCTION

Minimizing the use of animals in biomedical research is a crucial consideration due to the necessity of reusing animals in subsequent experiments. The animals available for reuse have undergone partial damage from previous treatments at various times, leading to carryover effects in subsequent experimentation. These effects, unfortunately, cannot be entirely eradicated. One strategy to mitigate the impact of partial damage in subsequent experiments is to incorporate previous treatments as covariates during the statistical analysis phase. Another approach involves designing experiments in a manner that maintains a nearly equal degree of damage. For instance, in the case of treatments involving drug doses, ensuring nearly equal damage implies that the cumulative dose for experimental units remains constant or nearly constant over time. Consequently, the experimental design should aim to keep the block sums constant. For example, if we have six doses of a drug with quantities $D_1$ (10ml), $D_2$ (20ml), $D_3$ (30ml), $D_4$ (40ml), $D_5$ (50ml) and $D_6$ (60ml) and want to conduct experiments on animals such that each animal is equally (or nearly equally) affected, we can use the following arrangements shown in Table 1 as:

This arrangement balances the cumulative doses across all animals, ensuring that each animal receives an equivalent total dose by the end of the experiment.

Naturally, balanced incomplete block designs (Dey, 1986) are simpler than the partially balanced incomplete block designs and as such preferred for the purpose of designing the experiments. This note addresses the issues pertaining to the existence of constant block sum BIBD. But Khattree (2018a) proved that, in general no such design exists. However, Khattree (2018b) does provide a particular constant block-sum PBIBD with four associate classes PBIBD (v = 16, b = 36, k = 4, r = 9, $(\lambda_1, \lambda_2, \lambda_3, \lambda_4)$ = (0, 3, 2, 3), (n1, n2, n3, n4) = (4, 1, 6, 4) by using famous Parshavnath Yantram, 4×4 magic square with enormous configurations leading to a constant sum of 34. Khattree (2019) presented constant block-sum PBIBD using of magic squares, special case of Parshvanath yantram, singular group divisible designs, paired sums, circular arrangement, magic circles and magic oblongs. Other researchers like Bansal and Garg (2020) also discussed the existence of constant block-sum PBIB designs and developed some construction methods using regular figures like concentric circle reticles and two- dimensional t-level segmented pyramids. Yadav *et al.* (2024) also proposed three construction methods by using Petersen Graph, Pappus Graph and Hexagon Graph. Further, Varghese *et al.* (2020), Karmakar *et al.* (2022), Vinayaka *et al.* (2024), Adeleke *et al.* (2024), Khattree (2023), Vinaykumar *et al.* (2023) and Yadav *et al.* (2024) discussed about incomplete block designs and constant block-sum PBIBD and have proposed some construction methods for same. In this study, we have developed two construction methods of constant block sum PBIBD by using tetrahedral and

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cubical association scheme proposed by Sharma *et al.* (2010). This research contributes to the development of experimental designs that allow for the reuse of animals while effectively managing the effects of previous treatments.

## MATERIALS AND METHODS

### Tetrahedral association scheme (Sharma *et al.,* 2010)

Arrange v=6t treatments on the edges of a tetrahedron such that each edge contains exactly t distinct treatments, then two treatments are

i) First associate if they belong to the same edge.

ii) Second associate if they belong to any of the edges that pass through the two vertices located on the edge.

iii) Third associate, otherwise.

The parameters of the association scheme are:

$$v = 6t,\ n_1 = t_1 - 1,\ n_2 = 4t,\ n_3 = t, \text{ and}$$

$$P_1 = \begin{pmatrix} t-2 & 0 & 0 \\ 0 & 6t & 0 \\ 0 & 0 & t \end{pmatrix}, P_2 = \begin{pmatrix} 0 & t-1 & 0 \\ t-1 & 4t & t \\ 0 & t & 0 \end{pmatrix}, P_3 = \begin{pmatrix} 0 & 0 & t-1 \\ 0 & 6t & 0 \\ t-1 & 0 & 6 \end{pmatrix}$$

By using this association scheme, we have developed a construction method for constructing constant block-sum PBIB designs as follows:

### Construction of three associate class design using tetrahedral

A tetrahedron has four triangular faces and six edges, each face bounded by the three edges. The t (even) treatments are found using $\frac{t}{2}$ sets of paired sums (have a constant sum) of 6 t treatments and putted on the all six edges. Form the four blocks of the design each one corresponding to a triangular face by taking together the treatments that lie on the three edges of the face as the block contents. The parameters of the design are:

$$(v=6t, b=4, r=2, k=3t\ \lambda_1=2,\ \lambda_2=1 \text{ and } \lambda_3=0)$$

with constant block sum $\frac{3t(1+6t)}{2}$

**Example 1:** For t=2 following sets of treatments:

$$\begin{cases}1\\12\end{cases} \begin{cases}2\\11\end{cases} \begin{cases}3\\10\end{cases} \begin{cases}4\\9\end{cases} \begin{cases}5\\8\end{cases} \text{and} \begin{cases}6\\7\end{cases}$$

are placed on tetrahedral as given in Fig 1.

Block of design are shown in table 2 with parameters

$$(v=12, b=4, r=2, k=6, \lambda_1=2, \lambda_2=1 \text{ and } \lambda_3=0)$$

and constant block sum 39.

Association scheme of the design presented in Table 2 is given in Table 3:

with parameters $v=12, n_1=1, n_2=8, n_3=2$

$$P_1 = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 8 & 0 \\ 0 & 0 & 2 \end{pmatrix}, P_2 = \begin{pmatrix} 0 & 1 & 0 \\ 1 & 4 & 2 \\ 0 & 2 & 0 \end{pmatrix}, P_3 = \begin{pmatrix} 0 & 0 & 1 \\ 0 & 8 & 0 \\ 1 & 0 & 0 \end{pmatrix}$$

### Construction of three associate class design using cubical association scheme

### Cubical association scheme (Sharma *et al.,* 2010)

Let the number of treatments be v = 8t (t≥2). Arrange these *v* treatments on the eight vertices of a cube such that each vertex contains exactly distinct treatments, then two treatments are:

**Table 1:** Arrangements of treatments in blocks.

| Animals (blocks) | Doses given (in ml) | Total (in ml) |
|---|---|---|
| 1 | $D_1$ (10), $D_6$ (60), $D_3$ (30), $D_4$ (40) | 140 |
| 2 | $D_2$ (20), $D_5$ (50), $D_1$ (10), $D_6$ (60) | 140 |
| 3 | $D_3$ (30), $D_4$ (40), $D_2$ (20), $D_5$ (50) | 140 |

**Table 2:** Constant block-sum PBIBD.

| Blocks | Block contents |
|---|---|
| I | (1,12,2,11,3,10) |
| II | (1,12,4,9,5,8) |
| III | (2,11,6,7,4,9) |
| IV | (3,10,5,8,6,7) |

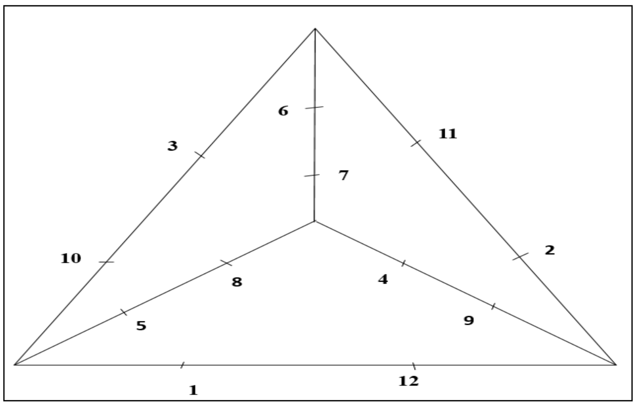


**Fig 1:** Arrangement of treatments on tetrahedral structure.

**Table 3:** Association Scheme.

| Treatments | First associates | Second associates | Third associates |
|---|---|---|---|
| 1 | 12 | 2,3,4,5,8,9,10,11 | 6,7 |
| 2 | 11 | 1,3,4,6,7,9,10,12 | 5,8 |
| 3 | 10 | 1,2,5,6,7,8,11,12 | 4,9 |
| 4 | 9 | 1,2,5,6,7,8,11,12 | 3,10 |
| 5 | 8 | 1,3,4,6,7,9,10,12 | 2,11 |
| 6 | 7 | 2,3,4,5,8,9,10,11 | 1,12 |
| 7 | 6 | 2,3,4,5,8,9,10,11 | 1,12 |
| 8 | 5 | 1,3,4,6,7,9,10,12 | 2,11 |
| 9 | 4 | 1,2,5,6,7,8,11,12 | 3,10 |
| 10 | 3 | 1,2,5,6,7,8,11,12 | 4,9 |
| 11 | 2 | 1,3,4,6,7,9,10,12 | 5,8 |
| 12 | 1 | 2,3,4,5,8,9,10,11 | 6,7 |

**Table 4:** Constant block-sum PBIBD.

| Blocks | Block contents |
|---|---|
| I | (1,16,2,15,4,13,5,12) |
| II | (2,15,1,16,3,14,6,11) |
| III | (3,14,2,15,4,13,7,10) |
| IV | (4,13,1,16,3,14,8,9) |
| V | (5,12,1,16,6,11,8,9) |
| VI | (6,11,7,10,2,15,5,12) |
| VII | (7,10,6,118,9,3,14) |
| VIII | (8,9,4,13,5,12,7,10) |

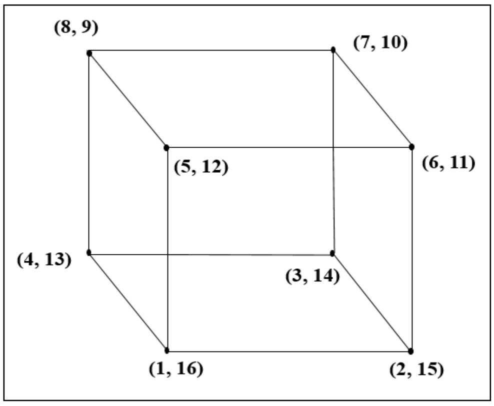

**Fig 2:** Arrangement of treatments on cubic structure.

i) First associates, if these lie on the same vertex.
ii) Second associates, if these lie on two different vertices except the diagonally opposite ones.
iii) Third associates, if these lie on diagonally opposite vertices.
The parameters of the association scheme are:

$$v = 8t, n_1 = t-1, n_2 = 6t, n_3 = t$$

$$P_1 = \begin{pmatrix} t-2 & 0 & 0 \\ 0 & 4t & 0 \\ 0 & 0 & t \end{pmatrix}, P_2 = \begin{pmatrix} 0 & t-1 & 0 \\ t-1 & 2t & t \\ 0 & t & 0 \end{pmatrix}, P_3 = \begin{pmatrix} 0 & 0 & t-1 \\ 0 & 4t & 0 \\ t-1 & 0 & 6 \end{pmatrix}$$

By using this association scheme, we have developed following construction method for constructing constant block-sum PBIB designs:

**Construction of three associate class design using cubic structure**

The t - tuple coordinates having a constant sum found using sets of paired sums with v=8t treatments (t should be even) and putted on the vertices of cubic structure. Now form the contents of a block by taking treatments that lie on a specific vertex and also on the other three vertices lying on the edges passing through the specific vertex. Likewise, obtain the other seven blocks corresponding to the remaining vertices of the cube. The eight blocks thus obtained, each corresponding to one vertex of the cube, form a constant block sum PBIB design based on the cubical association scheme with the parameters:

$$v = 8t, b = 8, r = 4, k = 4t, \lambda_1 = 4, \lambda_2 = 2, \lambda_3 = 0$$

with constant block sum 2 t (1 + 8t)

**Example 2:** For t=2 following sets of treatments

$$\left\{\begin{matrix}1\\16\end{matrix}\right. \left\{\begin{matrix}2\\15\end{matrix}\right. \left\{\begin{matrix}3\\14\end{matrix}\right. \left\{\begin{matrix}4\\13\end{matrix}\right. \left\{\begin{matrix}5\\12\end{matrix}\right. \left\{\begin{matrix}6\\11\end{matrix}\right. \left\{\begin{matrix}7\\10\end{matrix}\right. \text{and} \left\{\begin{matrix}8\\9\end{matrix}\right.$$

are placed on cubic structure shown in Fig 2:

Blocks of design obtained by the arrangement of treatments on cubic structure as given in Fig 2 are given in Table 4:

with parameters $v = 16, b = 8, r = 4, k = 8, \lambda_1 = 4, \lambda_2 = 2$ and $\lambda_3 = 0$ and constant block sum 68.

Association scheme of the design given in Table 4 is shown in Table 5:

with parameters $v = 16, n_1 = 1, n_2 = 12, n_3 = 2$

$$P_1 = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 12 & 0 \\ 0 & 0 & 2 \end{pmatrix}, P_2 = \begin{pmatrix} 0 & 1 & 0 \\ 1 & 8 & 2 \\ 0 & 2 & 0 \end{pmatrix}, P_3 = \begin{pmatrix} 0 & 0 & 1 \\ 0 & 12 & 0 \\ 1 & 0 & 0 \end{pmatrix}$$

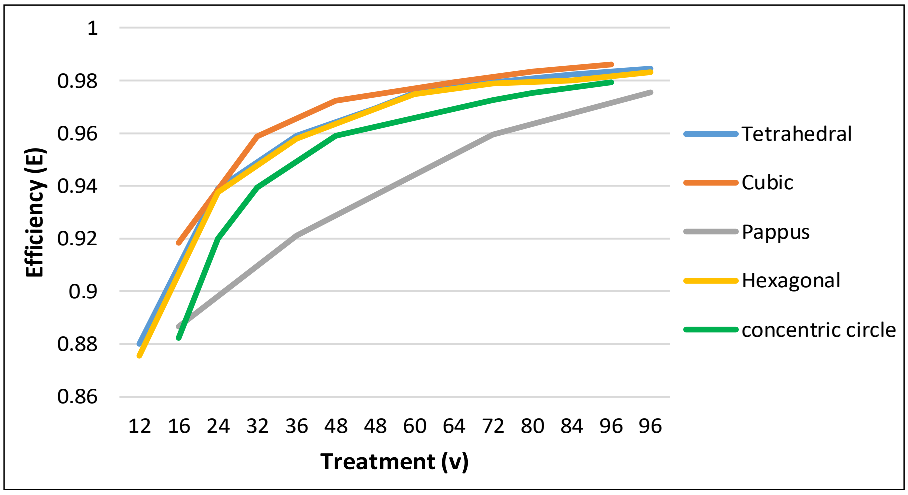


**Fig 3:** Comparison of proposed designs with existing designs w.r.t. efficiency.

**Table 5:** Association scheme.

| Treatments | First associates | Second associates | Third associates |
|---|---|---|---|
| 1 | 16 | 2,3,4,5,6,8,9,11,12,13,14,15 | 7,10 |
| 2 | 15 | 1,3,4,5,6,7,10,11,12,13,14,16 | 8,9 |
| 3 | 14 | 1,2,4,6,7,8,9,10,11,13,15,16 | 5,12 |
| 4 | 13 | 1,2,3,5,7,8,9,10,12,14,15,16 | 6,11 |
| 5 | 12 | 1,2,4,6,7,8,9,10,11,13,15,16 | 3,14 |
| 6 | 11 | 1,2,3,5,7,8,9,10,12,14,15,16 | 4,13 |
| 7 | 10 | 2,3,4,5,6,8,9,11,12,13,14,15 | 1,16 |
| 8 | 9 | 1,3,4,5,6,7,10,11,12,13,14,16 | 2,15 |
| 9 | 8 | 1,3,4,5,6,7,10,11,12,13,14,16 | 2,15 |
| 10 | 7 | 2,3,4,5,6,8,9,11,12,13,14,15 | 1,16 |
| 11 | 6 | 1,2,3,5,7,8,9,10,12,14,15,16 | 4,13 |
| 12 | 5 | 1,2,4,6,7,8,9,10,11,13,15,16 | 3,14 |
| 13 | 4 | 1,2,3,5,7,8,9,10,12,14,15,16 | 6,11 |
| 14 | 3 | 1,2,4,6,7,8,9,10,11,13,15,16 | 5,12 |
| 15 | 2 | 1,3,4,5,6,7,10,11,12,13,14,16 | 8,9 |
| 16 | 1 | 2,3,4,5,6,8,9,11,12,13,14,15 | 7,10 |

**Table 6:** List of possible constant block-sum PBIB designs from proposed methods.

| v | b | r | k | $\lambda_1$ | $\lambda_2$ | $\lambda_3$ | $n_1$ | $n_2$ | $n_3$ | E | Association scheme based on |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 12 | 4 | 2 | 6 | 2 | 1 | 0 | 1 | 8 | 2 | 0.8800 | Tetrahedral structure |
| 16 | 8 | 4 | 8 | 4 | 2 | 0 | 1 | 12 | 2 | 0.9184 | Cubic structure |
| 24 | 4 | 2 | 12 | 2 | 1 | 0 | 3 | 16 | 4 | 0.9388 | Tetrahedral structure |
| 32 | 8 | 4 | 16 | 4 | 2 | 0 | 3 | 24 | 4 | 0.9588 | Cubic structure |
| 36 | 4 | 2 | 18 | 2 | 1 | 0 | 5 | 24 | 6 | 0.9589 | Tetrahedral structure |
| 48 | 8 | 4 | 24 | 4 | 2 | 0 | 5 | 36 | 6 | 0.9724 | Cubic structure |
| 48 | 4 | 2 | 24 | 2 | 1 | 0 | 7 | 32 | 8 | 0.9691 | Tetrahedral structure |
| 60 | 4 | 2 | 30 | 2 | 1 | 0 | 9 | 40 | 10 | 0.9752 | Tetrahedral structure |
| 64 | 8 | 4 | 32 | 4 | 2 | 0 | 7 | 48 | 8 | 0.9793 | Cubic structure |
| 72 | 4 | 2 | 36 | 2 | 1 | 0 | 11 | 48 | 12 | 0.9793 | Tetrahedral structure |
| 80 | 8 | 4 | 40 | 4 | 2 | 0 | 9 | 60 | 10 | 0.9834 | Cubic structure |
| 84 | 4 | 2 | 42 | 2 | 1 | 0 | 13 | 56 | 14 | 0.9823 | Tetrahedral structure |
| 96 | 8 | 4 | 48 | 4 | 2 | 0 | 11 | 72 | 12 | 0.9862 | Cubic structure |
| 96 | 4 | 2 | 48 | 2 | 1 | 0 | 15 | 64 | 16 | 0.9845 | Tetrahedral structure |

## RESULTS AND DISCUSSION

A comprehensive list of constant block-sum PBIB designs has been compiled for cases where v<10 in Table 6. This list includes design parameters as well as efficiency (E) values in comparison to a randomized complete block design.

We have also compared proposed designs with existing designs developed by using concentric circle, Pappus graph and Hexagonal graph proposed by Bansal and Garg (2020) and Yadav *et al.* (2024). From the following graph, we can observe that the proposed designs (Cubic and Tetrahedral) are more efficient than the existing designs (Concentric Circle, Pappus Graph and Hexagonal Graph) as shown in Fig 3. Tetrahedral and Hexagonal-based designs exhibit nearly equal efficiency; however, Tetrahedral-based designs require fewer experimental units compared to Hexagonal-based designs, making them more resource-efficient.

## CONCLUSION

In this article, we have proposed two methods for constructing Constant block-sum PBIB designs which have more importance in dose-response studies in case of animal experiments where a particular animal is used to repeated measurements over a time period w.r.t. doses under investigation. The most advantage of these designs is that if we wish to do experiment in subsequence form, the set of experimental units used, as homogeneous and thus can reuse them in later subsequent experiments. As the view point of minimization of number of animals used, this issue is of an ever-increasing importance.

### Conflict of interest

The authors declare that there are no conflict of interest regardly the publication of this article.

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