Electronic Journal of Statistics Vol. 8 (2014) 2923–2936 ISSN: 1935-7524 DOI: 10.1214/14-EJS979

Construction of minimal balanced cross over designs having good efficiency of separability

Jyoti Divecha and Jignesh Gondaliya

Department of Statistics, Sardar Patel University Vallabh Vidyanagar, Gujarat-388120, India e-mail: j.divecha@yahoo.com; jjgondaliya@gmail.com

Abstract: Minimal balanced cross over designs having lesser, equal and more periods than the number of treatments are constructed using directed m-terraces and their modified forms. A complementary pair and trio of the terraces constructs a cross over design with lesser periods while a uniform terrace yields a uniform cross over design. Two new series of cross over designs in even number of treatments have been obtained. All the designs possess good efficiency of separability and therefore they are suitable for the estimation of direct and first order carry over effects of treatments. A list of terraces for the construction of minimal balanced cross over designs having three to nine treatments is given.

MSC 2010 subject classifications: Primary 62K05, 62K25; secondary 62K10.

Keywords and phrases: Cross over, direct effect, minimal, directed mterrace, carry over effect.

Received September 2013.

Contents

1	Intro	$\operatorname{pduction}$	2924
2	Preli	iminaries and new definitions	2925
	2.1	Model of $COD(t, n, p)$	2925
	2.2	Characterization of COD	2925
	2.3	Definitions of terraces	2926
3	Metl	hod of construction	2927
	3.1	Minimal balanced $COD(t, n, p(< t))$	2927
	3.2	Minimal balanced $COD(t, t, t)$	2931
	3.3	Minimal balanced $COD(t, t, p(>t))$	2932
4	Cone	clusion	2934
Ap	pend	ix	2934
Re	feren	ces	2935

1. Introduction

An experimental design in which experimental units (subjects) are used repeatedly by exposing them to a sequence of treatments is called a cross over design (*COD*). Each experimental unit is influenced by the direct effect of the treatments applied and by the carry over effect of the previously applied treatments. These cross over designs also known as change over designs and sometimes as repeated measurements designs, have been discussed by many authors under different assumptions. Significant contributions are due to Grizzle [10], Blaisdell and Raghavaravo [3], Dey et al. [7], Fletcher [8], Kunert [17], Senn [23], Carriere [4], Collombier and Merchermek [6], Jones and Donev [14], Vonesh and Chinchilli [25], Kushner [18], Martin and Eccleston [19], Jones and Kenward [13], Nason and Follmann [22] and others.

The main advantage of a COD is that the treatments are compared withinsubjects and such within-subject studies allow a more precise comparison of treatments. Some real life applications of the CODs are discussed by Taka and Armitage [24] and Matthews [20]. Literature review of the applications of the above three types of CODs indicated that each of them has specific applications. The CODs having lesser periods are suitable in clinical trials and pharmaceutical studies because each unit receives only a few of all the treatments. The CODs having periods equal to the number of treatments so that each unit receives every treatment once are employed in agriculture and for the sensory evaluation of food and products. The CODs having more periods than the number of treatments, so that a sequence of treatments including repetitions can be given are useful in animal nutrition and educational experiments (e.g., Gill [9]). Hedayat and Afsarinejad [12] emphasized on the construction of minimal size CODs, i.e., CODs which are balanced and require minimum possible number of experimental units for comparing a set of treatments.

Bailey [2] defined the terrace and used it for the construction of Quasicomplete Latin squares. Morgan [21] generalized the idea of terrace to m-terrace and used it for the construction of balanced polycross designs. The present paper introduces modified forms of terrace called complementary pair of terraces and complementary trio of terraces and provides a simple method for the construction of four series of minimal balanced CODs. Two series based on the modified forms of terrace are new series of CODs for even number of treatments in lesser periods. Some of the CODs of new series are strongly balanced CODs. The other two series of CODs are based on the directed m-terraces of Morgan [21]. Some of them are the same as those in Hedayat and Afsarinejad [12] and William [26], but our method of construction is quite simple and yields some better CODs.

The paper is organized as follows. The Section 2 presents the model considered for COD, characterization of COD and the definitions of terraces used in the paper. Construction of CODs is discussed in Section 3. It is shown that each of the four series is constructed using a common method but a specific terrace. Construction of each series is illustrated by examples. A comparison of CODs with those of Afsarinejad and Hedayat [1] in terms of efficiency of separability is

given. A list of directed 2-terraces, complementary pair of terraces and complementary trio of terraces for the construction of minimal balanced *CODs* having three to nine treatments is provided in the Appendix.

2. Preliminaries and new definitions

Throughout this paper, a COD in which t treatments are compared using n experimental units repeatedly measured for p periods is denoted by COD(t, n, p).

2.1. Model of COD(t, n, p)

The CODs considered in this paper are suitable for the estimation of direct and first order carry over effects. The direct effect is effect of a treatment in the period in which it is applied and the first order carry over effect is effect of a treatment in the period which was applied in the preceding period to the same unit. The model considered for the CODs is the most frequently used simple carry over model which was introduced by Hedayat and Afsarinejad [12] and it is given by,

$$\underline{Y} = \underline{1}\mu + T\underline{\tau} + R\gamma + P\underline{\alpha} + U\beta + \underline{\varepsilon}, \qquad (2.1)$$

where \underline{Y} is the vector of responses ordered as $(Y_{11}, \ldots, Y_{p1}, Y_{12}, \ldots, Y_{p2}, \ldots, Y_{1n}, \ldots, Y_{pn})$, μ is the general effect, $\underline{\tau}, \underline{\gamma}, \underline{\alpha}, \underline{\beta}$ are respectively the vectors of direct treatment effects, first order carry over effects, period effects and unit effects. T is the observation-direct treatment incidence matrix, R is the observation-first order carry over treatment incidence matrix, P is the observation-period incidence matrix given by $I_n \otimes J_{p,1}$. U is the observation-unit incidence matrix given by $J_{n,1} \otimes I_p$. The vector $\underline{\varepsilon}$ is normally distributed errors with mean zero and variance-covariance matrix $\sigma^2 I$.

2.2. Characterization of COD

Definition 2.1. A COD(t, n, p) is said to be *balanced* with respect to the set of direct and first order carry over effects if (i) in each period, each treatment is given to λ_1 units, and (ii) in two successive periods, each ordered pair of distinct treatments is given to λ_2 units, while, each pair of treatments with itself is given to λ_3 units, where integer λ_1 , λ_2 are positive and λ_3 is non-negative.

Consequently, a balanced COD satisfies the following parametric relations,

$$n = \lambda_1 t, \tag{2.2}$$

$$n(p-1) = (\lambda_2(t-1) + \lambda_3)t.$$
(2.3)

A minimal COD is a design in which the number of units that receive each treatment in each period (λ_1) is as small as possible. From (2.2) and (2.3), Definition 2.2 follows.

Definition 2.2. A balanced COD(t, n, p) is said to be *minimal* if λ_1 is the smallest integer such that

$$(\lambda_1(p-1) - \lambda_3) \equiv 0(modulo(t-1)). \tag{2.4}$$

A balanced COD is said to be strongly balanced whenever λ_3 equals λ_2 . A COD is called uniform over experimental units if each treatment is applied equally frequently to each experimental unit. A COD is called uniform over periods if each treatment occur equally frequently in each period. A balanced COD is always uniform over periods. Therefore, a balanced COD uniform over experimental units is called uniform COD.

A COD for model 2.1 must be characterized for its ability of separating the direct and first order carry over effects. A measure of separability called efficiency of separability (ES) of COD is calculated on the basis of observed frequencies of first order carry over and the expected frequencies from an independent model. Following Hanford [11], a measure of ES of direct and first order carry over effects for balanced CODs is calculated by

$$ES = \left[1 - \left\{\frac{(\lambda_3 - \lambda_2)^2}{(\lambda_3 + (t-1)\lambda_2)(\lambda_1 + \lambda_3 + (t-1)\lambda_2)}\right\}^{\frac{1}{2}}\right] \times 100\%.$$
 (2.5)

For example, the ES of the $COD\{AB, BA\}$ calculated by substituting $\lambda_1 = 1$, $\lambda_2 = 1$ and $\lambda_3 = 0$ in the equation (2.5) is 29%, while the ES of the $COD\{AB, BA, AA, BB\}$ obtained by substituting $\lambda_1 = 1$, $\lambda_2 = 1$ and $\lambda_3 = 1$ is 100%. The low ES indicates unsuitability while the high ES indicates suitability of COD for the estimation of direct and first order carry over effect of treatments under model 2.1.

2.3. Definitions of terraces

Let Z_t be a group of order t with elements $0, 1, \ldots, t-1$. Let $x = (x_1, x_2, \ldots, x_p)$ be some arrangement of the elements of group Z_t with both repeats and nonoccurrences allowed. Corresponding to each such x, let x^* be the arrangement $(x_2 - x_1, x_3 - x_2, \ldots, x_p - x_{p-1})$. Note that, the successive repeats of elements in x contribute to the value of λ_3 (i.e., count of zero in x^*).

Definition 2.3. An arrangement $a = (a_1, a_2, \ldots, a_p)$ of p elements of Z_t where $p = 1 + \frac{m(t-1)}{2}$ for some positive even integer m is said to be a *directed m-terrace* if a^* modulo t consists of each non zero element of Z_t exactly m/2 times.

For example, consider an arrangement a = (0, 1, 3, 2, 3, 1, 0, 2, 3, 2) from the group of order 4, i.e., $Z_4 = \{0, 1, 2, 3\}$. Then $a^* = (1, 2, -1, 1, -2, -1, 2, 1, -1)$ and a^* modulo 4 is (1, 2, 3, 1, 2, 3, 2, 1, 3) because $1 \equiv -3$ (modulo 4), $2 \equiv -2$ (modulo 4) and $3 \equiv -1$ (modulo 4). Here, a^* modulo 4 consists of each non zero element of Z_4 exactly 3 times and hence a is a directed 6-terrace. Using this idea of directed m-terrace, three new forms of terraces, namely, uniform 2-terrace, complementary pair of terraces and complementary trio of terraces are defined.

Definition 2.4. A directed 2-terrace over Z_t for even t is said to be a *uniform* 2-terrace if it consists of all the elements of Z_t once.

For example, a directed 2-terrace a = (0, 1, 3, 2) over Z_4 is a uniform 2-terrace because it contains all the elements of Z_4 once. A list of directed 2-terraces with uniform 2-terraces from groups of order three to eight is provided in Table 3 (Appendix).

Definition 2.5. A pair of arrangements $a = (a_1, a_2, \ldots, a_p)$ and $b = (b_1, b_2, \ldots, b_p)$ of the elements of Z_t , where $p = int(\frac{t}{2}) + 1$ is said to be a *complementary* pair of terraces if (a^*, b^*) modulo t consists of each non zero element of Z_t once, for odd t, while, each element of Z_t once, for even t.

For example, a pair of arrangements a = (0, 3, 1) and b = (2, 3, 3) from $Z_4 = \{0, 1, 2, 3\}$ is a complementary pair of terraces because (a^*, b^*) modulo 4 is (3,2,1,0). A list of complementary pair of terraces from groups of order three to nine is provided in Table 4 (Appendix).

Definition 2.6. A trio of arrangements $a = (a_1, a_2, \ldots, a_p)$, $b = (b_1, b_2, \ldots, b_p)$ and $c = (c_1, c_2, \ldots, c_p)$ of the elements of Z_t for even $t \ge 4$, where $p = \frac{t}{2}$ is said to be a *complementary trio of terraces* if (a^*, b^*, c^*) modulo t consists of each non zero element of Z_t once and zero element $\frac{3}{2}(t-2) - (t-1)$ times.

For example, a trio of arrangements a = (0, 1), b = (1, 0) and c = (0, 2) from $Z_4 = \{0, 1, 2, 3\}$ is a complementary trio of terraces because (a^*, b^*, c^*) modulo 4 is (1,3,2). A list of complementary trio of terraces from groups of order four to eight is provided in Table 5 (Appendix).

3. Method of construction

In this section, two series of minimal balanced COD(t, n, p(< t)), and one series each of minimal balanced COD(t, t, t) and minimal balanced COD(t, n, p(> t))are constructed using a simple method of construction. It is shown that, the simple method of construction applied on a specific form of terraces results in a specific series of CODs.

3.1. Minimal balanced COD(t, n, p(< t))

In several experimental situations, it is not convenient to measure each experimental unit for all treatments, especially when the number of treatments is large. Balanced CODs in which each experimental unit is measured only for fractions of all treatments is desirable.

Theorem 3.1. A series of minimal balanced $COD(t, 2t, int(\frac{t}{2}) + 1)$ can be constructed by adding successively each element of Z_t to a complementary pair of terraces reduced modulo t.

Proof. Consider a complementary pair of terraces $a = (a_1, a_2, \ldots, a_p)$ and $b = (b_1, b_2, \ldots, b_p)$ with $p = int(\frac{t}{2}) + 1$, as two adjacent columns [a' : b']. Adding

successively each element of Z_t to [a':b'] reduced modulo t gives a $p \times 2t$ array,

$$\begin{bmatrix} a_{1}+0 & b_{1}+0 & a_{1}+1 & b_{1}+1 & \cdots & a_{1}+(t-1) & b_{1}+(t-1) \\ a_{2}+0 & b_{2}+0 & a_{2}+1 & b_{2}+1 & \cdots & a_{2}+(t-1) & b_{2}+(t-1) \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ a_{p}+0 & b_{p}+0 & a_{p}+1 & b_{p}+1 & \cdots & a_{p}+(t-1) & b_{p}+(t-1) \end{bmatrix}$$
modulo t .

Now, considering the rows of the above array as periods and the columns as units constructs the said COD because, from the definition of complementary pair of terraces, $\lambda_3 = 1$ for even t and $\lambda_3 = 0$ for odd t, and hence from the equations (2.2)–(2.3), $\lambda_1 = 2$ and $\lambda_2 = 1$. Then from the equation (2.4), the COD is minimal balanced.

Example 3.1. To construct COD(4, 8, 3), consider the group $Z_4 = \{0, 1, 2, 3\}$. Define a complementary pair of terraces such as a = (0, 3, 1) and b = (2, 3, 3). Consider them as two adjacent columns,

$$\begin{array}{ccc}
 0 & 2 \\
 3 & 3 \\
 1 & 3
 \end{array}$$

Adding successively 0, 1, 2 and 3 to the above columns reduced modulo 4 constructs the minimal balanced COD(4, 8, 3) given by

			Experimental units									
		$\begin{array}{cccccccccccccccccccccccccccccccccccc$										
	1	0	2	1	3	2	0	3	1			
Periods	2	3	3	0	0	1	1	2	2			
	3	1	3	2	0	3	1	0	2			

Note that, $\lambda_1 = 2, \lambda_2 = 1, \lambda_3 = 1$ and ES = 100%.

Example 3.2. To construct COD(6, 12, 4), consider the group $Z_6 = \{0, 1, \ldots, 5\}$. Define a complementary pair of terraces such as a = (2, 0, 1, 4) and b = (5, 1, 0, 0). Consider them as two adjacent columns [a' : b']. Adding successively 0, 1, 2, 3, 4 and 5 to [a' : b'] reduced modulo 6 constructs the minimal balanced COD(6, 12, 4) given by

			Experimental units											
		1	1 2 3 4 5 6 7 8 9 10 11 12											
	1	2	5	3	0	4	1	5	2	0	3	1	4	
Periods	2	0	1	1	2	2	3	3	4	4	5	5	0	
	3	1	0	2	1	3	2	4	3	5	4	0	5	
	4	4	0	5	1	0	2	1	3	2	$ \begin{array}{c} 3 \\ 5 \\ 4 \\ 4 \end{array} $	3	5	

Note that, $\lambda_1 = 2, \lambda_2 = 1, \lambda_3 = 1$ and ES = 100%.

Example 3.3. To construct COD(7, 14, 4), consider the group $Z_7 = \{0, 1, \ldots, 6\}$. Define a complementary pair of terraces such as a = (0, 1, 3, 6) and b = (0, 6, 4, 1). Consider them as two adjacent columns [a' : b']. Adding successively 0, 1, 2, 3, 4, 5 and 6 to [a' : b'] reduced modulo 7 constructs the minimal balanced

			Experimental units												
		1	1 2 3 4 5 6 7 8 9 10 11 12 13 14												
	1	0	0	1	1	2	2	3	3	4	4	5	5	6	6
Periods	2	1	6	2	0	3	1	4	2	5	3	6	4	0	5
	3	3	4	4	5	5	6	6	0	0	1	1	2	2	3
	4	6	1	0	2	1	3	2	4	3	5	4	5 4 2 6	5	0

Note that, $\lambda_1 = 2, \lambda_2 = 1, \lambda_3 = 0$ and ES = 86%.

Remark 3.1. Some minimal balanced CODs with p < t, t odd, provides balanced incomplete block designs for nearest neighbor model (EBIBD) (for details see Kiefer and Wynn [15]). Example 3.3 is EBIBD(7,14,8,4,4).

Theorem 3.2. A series of minimal balanced $COD(t, 3t, \frac{t}{2})$ for even $t(\geq 4)$ can be constructed by adding successively each element of Z_t to a complementary trio of terraces reduced modulo t.

Proof. Consider a complementary trio of terraces $a = (a_1, a_2, \ldots, a_p)$, $b = (b_1, b_2, \ldots, b_p)$ and $c = (c_1, c_2, \ldots, c_p)$ with $p = \frac{t}{2}$, as three adjacent columns [a': b': c']. Adding successively each element of Z_t to [a': b': c'] reduced modulo t form a $p \times 3t$ array. Now, considering the rows of the array as periods and the columns as units constructs the said COD because, from the definition of complementary trio of terraces, $\lambda_3 = \frac{3}{2}(t-2) - (t-1)$, and hence from the equations (2.2)-(2.3), $\lambda_1 = 3$ and $\lambda_2 = 1$. Then from the equation (2.4), the COD is minimal balanced.

Table 1 lists ES calculated using equation (2.5) of CODs having three to ten treatments and three to thirty units for with and without repetition of the last period. As per our literature search so far no strongly balanced CODs are available for even number of treatments in $\frac{t}{2} + 1$ periods. Theorem 3.1 can be used to construct such CODs, because any complementary pair of terraces for even t, necessarily hold $\lambda_3 = \lambda_2 = 1$. One more strongly balanced COD, COD(6, 18, 3) can be constructed using Theorem 3.2 owing to incidental equality of λ_2 and λ_3 . Table 1 shows five new strongly balanced CODs, COD(4, 8, 3), COD(6, 12, 4), COD(6, 18, 3), COD(8, 16, 5) and COD(10, 20, 6). Afsarinejad and Hedayat [1] have especially considered two periods CODs for comparing t treatments. Their CODs has several units which do not receive cross over treatments, i.e., same treatment is given twice. Table 2 provides ES of Afsarinejad and Hedayat [1] two period *CODs* and alternative useful *CODs* of this paper. Table 2 shows that, the COD(t, n, p(< t)) are better alternative to their two period designs. In particular, the COD(5, 15, 2) of Afsarinejad and Hedayat [1] and this paper COD(5, 10, 3), both uses equal 30 number of observations and the latter COD possesses higher ES. Further, Table 1 shows that, the ES for the $COD(t, 2t, int(\frac{t}{2}) + 1)$ for odd t constructed using Theorem 3.1, improves when the last period is repeated. Note that, the ES improves considerably for the COD with three treatments, COD(3, 6, 2) has 65% ES while, COD(3, 6, 3)has 80% ES.

		Without Re	neating	With Rep	peating
		last per		last pe	
t	n	p	ES	p p	ES
3	3	3	59	4	100
	3	5	55	6	82
	6	2	65	3	80
4	4	4	71	5	100
	8	3	100*	_	_
	12	2	76^{*}	-	-
	4	7	69	8	87
	4	10	68	11	81
5	5	5	78	6	100
	10	3	80	4	86
	5	9	76	10	86
6	6	6	82	7	100
	12	4	100^{*}	-	-
	18	3	100^{*}	-	-
7	7	7	85	8	100
	14	4	86	5	89
8	8	8	87	9	100
	16	5	100^{*}	-	-
	24	4	90^{*}	-	-
9	9	9	88	10	100
	18	5	89	6	91
10	10	10	89	11	100
	20	6	100^{*}	-	-
	30	5	85^{*}	-	-
* i	ndicate	the new COD.			

		TABLE 1			
ES of COD	with and	d without	repeating	last period	

Afsarinejad & He	dayat [1]	Our paper					
Design	ES	Design	\mathbf{ES}				
COD(3, 6, 2)	65	COD(3, 6, 2)	65				
COD(4, 8, 2)	59	COD(4,8,3)	100				
		COD(4, 12, 2)	76				
COD(5,15,2) D1	71	COD(5,10,3)	80				
D2	68						
D3	71						
D4	63						
COD(6, 18, 2)	68	COD(6, 12, 4)	100				
		COD(6, 18, 3)	100				
COD(7,21,2)	68	COD(7, 14, 4)	86				
COD(7, 28, 2)	75						
COD(8, 56, 2)	67	COD(8, 16, 5)	100				
		COD(8, 24, 4)	90				
COD(10,90,2)	70	COD(10,20,6)	100				
		COD(10, 30, 5)	85				

 $\begin{array}{c} {\rm TABLE \ 2} \\ ES \ of \ Afsarine jad \ \& \ Hedayat \ [1] \ COD \ comparable \ to \ our \ COD \ with \ p < t \end{array}$

Example 3.4. To construct COD(4, 12, 2), consider the group $Z_4 = \{0, 1, 2, 3\}$. Define a complementary trio of terraces such as a = (0, 1), b = (1, 0) and c = (0, 2). Consider them as three adjacent columns [a' : b' : c']. Adding successively

0, 1, 2 and 3 to [a':b':c'] reduced modulo 4 constructs the minimal balanced COD(4, 12, 2) given by

			Experimental units											
		1	1 2 3 4 5 6 7 8 9 10 11 12											
Periods	1	0	1	0	1	2	1	2	3	2	3	0	3	
	2	1	0					3		0	0	3	1	

Note that, $\lambda_1 = 3$, $\lambda_2 = 1$, $\lambda_3 = 0$ and ES = 76%. A comparative COD(4, 8, 2) in Table 2 has lower ES (59%) as λ_2 is not constant.

Example 3.5. To construct COD(6, 18, 3), consider the group $Z_6 = \{0, 1, 2, 3, 4, 5\}$. Define a complementary trio of terraces such as a = (2, 0, 1), b = (3, 0, 5) and c = (4, 0, 0). Consider them as three adjacent columns [a' : b' : c']. Adding successively 0, 1, 2, 3, 4 and 5 to [a' : b' : c'] reduced modulo 6 constructs the minimal balanced COD(6, 18, 3) given by

		Experimental units																
Periods																		
1	2	3	4	3	4	5	4	5	0	5	0	1	0	1	2	1	2	3
2	0	0	0	1	1	1	2	2	2	3	3	3	4	4	4	5	5	5
$\begin{array}{c} 1\\ 2\\ 3\end{array}$	1	5	0	2	0	1	3	1	2	4	2	3	5	3	4	0	4	5

Note that, $\lambda_1 = 3, \lambda_2 = 1, \lambda_3 = 1$ and ES = 100%.

3.2. Minimal balanced COD(t, t, t)

When it is possible to measure each experimental unit repeatedly for t times, a minimal balanced COD(t, t, t) is suitable. This design is constructed using a directed 2-terrace.

Theorem 3.3. A series of minimal balanced COD(t, t, t) can be constructed by adding successively each element of Z_t to a directed 2-terrace reduced modulo t.

Proof. Consider a directed 2-terrace $a = (a_1, a_2, \ldots, a_p)$ with p = t, as a column a'. Adding successively each element of Z_t to a' reduced modulo t form a $p \times t$ array. Now, considering the rows of the array as periods and the columns as units constructs the said COD because, from the definition of directed 2-terrace, $\lambda_3 = 0$, and hence from the equations (2.2)–(2.3), $\lambda_1 = 1$ and $\lambda_2 = 1$. Then from the equation (2.4), the COD is minimal balanced.

From equation (2.5) and Table 1, it is clear that, the ES of COD(t, t, t) increases with t and it is reasonably high (more than 75%) for $t \ge 5$. COD(t, t, t) for even t are the same as those given in William [26]. Cheng and Wu [5] have shown that COD(t, t, t) becomes COD(t, t, t + 1) when last period is repeated, is optimal for the estimation of direct and first order carry over effects, which in terms of ES means, ES is necessarily 100%.

Example 3.6. To construct COD(6, 6, 6), consider the group $Z_6 = \{0, 1, 2, 3, 4, 5\}$. Define a directed 2-terrace such as a = (0, 4, 5, 2, 1, 3). Consider column a' as a

sequence for the first unit. Adding successively 0, 1, 2, 3, 4 and 5 to a' reduced modulo 6 constructs the minimal balanced COD(6, 6, 6) given by

		Experimental units									
		1	2	3	4	5	6				
	1	0	1	2	3	4	5				
	2	4	5	0	1	2	3				
Periods	3	5	0	1	2	3	4				
	4	2	3	4	5	0	1				
	5	1	2	3	4	5	0				
	6	3	4	5	0	1	2				

Note that, $\lambda_1 = 1, \lambda_2 = 1$ and $\lambda_3 = 0$. ES of this design is 82% and that of minimal balanced COD(6, 6, 7) is 100%.

Remark 3.2. Minimal balanced CODs obtained using uniform 2-terrace will be uniform and hence, following Kunert [16] they are universally optimal for the estimation of direct effects (e.g. Example 3.6).

Example 3.7. To construct COD(7,7,7), consider the group $Z_7 = \{0, 1, 2, 3, 4, 5, 6\}$. Define a directed 2-terrace such as a = (0, 1, 3, 6, 3, 1, 0). Consider column a' as a sequence for the first unit. Adding successively 0, 1, 2, 3, 4, 5 and 6 to a' reduced modulo 7 constructs the minimal balanced COD(7,7,7) given by

		Experimental units								
		1	2	3	4	5	6	7		
	1	0	1	2	3	4	5	6		
	2	1	2	3	4	5	6	0		
	3	3	4	5	6	0	1	2		
Periods	4	6	0	1	2	3	4	5		
	5	3	4	5	6	0	1	2		
	6	1	2	3	4	5	6	0		
	7	0	1	2	3	4	5	6		

Note that, $\lambda_1 = 1, \lambda_2 = 1$ and $\lambda_3 = 0$. ES of this design is 85% and that of minimal balanced COD(7, 7, 8) is 100%.

3.3. Minimal balanced COD(t, t, p(>t))

If an experimental situation demands minimal balanced COD with p > t, such design can be constructed by directed m-terrace.

Theorem 3.4. A series of minimal balanced $COD(t, t, 1 + \frac{m(t-1)}{2})$ for even $m(\geq 4)$ can be constructed by adding successively each element of Z_t to a directed *m*-terrace reduced modulo *t*.

Proof. Consider a directed m-terrace $a = (a_1, a_2, \ldots, a_p)$ with $p = 1 + \frac{m(t-1)}{2}$, as a column a'. Adding successively each element of Z_t to a' reduced modulo t form a $p \times t$ array. Now, considering the rows of the array as periods and the columns as units constructs the said COD because, from the definition of

directed m-terrace, $\lambda_3 = 0$, and hence from the equations (2.2)–(2.3), $\lambda_1 = 1$ and $\lambda_2 = \frac{m}{2}$. Then from the equation (2.4), the *COD* is minimal balanced.

From equation (2.5) and Table 1, it is clear that, in spite of a larger number of periods the ES is not much affected. Similar to other CODs, the ES improves with repetition of the last period. It is interesting to note that repeating the last period λ_2 times improves the ES to 100%.

Example 3.8. To construct COD(4, 4, 10), consider the group $Z_4 = \{0, 1, 2, 3\}$. Define a directed 6-terrace such as a = (0, 1, 3, 2, 3, 1, 0, 2, 3, 2). Consider column a' as a sequence for the first unit. Adding successively 0, 1, 2 and 3 to a' reduced modulo 4 constructs the minimal balanced COD(4, 4, 10) given by

		Experimental units							
		1	2	3	4				
	1	0	1	2	3				
	2	1	2	3	0				
	3	3	0	1	2				
	4	2	3	0	1				
Periods	5	3	0	1	2				
	6	1	2	3	0				
	7	0	1	2	3				
	8	2	3	0	1				
	9	3	0	1	2				
	10	2	3	0	1				

Note that, $\lambda_1 = 1, \lambda_2 = 3$ and $\lambda_3 = 0$. ES of this design is 68% and that of minimal balanced COD(4, 4, 11) is 81%.

Example 3.9. To construct COD(5, 5, 9), consider the group $Z_5 = \{0, 1, 2, 3, 4\}$. Define a directed 4-terrace such as a = (0, 4, 2, 3, 0, 1, 3, 2, 0). Consider column a' as a sequence for the first unit. Adding successively 0, 1, 2, 3 and 4 to a' reduced modulo 5 constructs the minimal balanced COD(5, 5, 9) given by

-

		Experimental units					
			1	2	3	4	5
	1		0	1	2	3	4
Periods	2		4	0	1	2	3
	3		2	3	4	0	1
	4		3	4	0	1	2
	5		0	1	2	3	4
	6		1	2	3	4	0
	7		3	4	0	1	2
	8		2	3	4	0	1
	9		0	1	2	3	4

Note that, $\lambda_1 = 1, \lambda_2 = 2$ and $\lambda_3 = 0$. ES of this design is 76% and that of minimal balanced COD(5, 5, 11) as COD(5, 5, 9) with repetition of last period twice is 100%.

4. Conclusion

The article presents a two step method to construct three types of minimal balanced cross over designs. A terrace is defined and then the group elements are added to it. The newly defined complementary terraces results in new series of minimal balanced cross over designs. All new minimal strongly balanced cross over designs with an even number of treatments are constructed using complementary terraces that contain successive repetitions of one group element. The efficiency of separability of our designs can be enhanced by extending the periods, sometime even to 100%. In the case of simple carry over model, if possible, one must prefer a three period cross over design over the two period designs.

Appendix

	of anecieu z-terraces with antiform z-terraces from groups of oraer 5 to 8
Group	Directed 2-terraces
Z_3	(0, 1, 0)
Z_4	(0,1,0,2), (0,1,3,2), (0,2,1,2), (0,2,3,2)
Z_5	(0, 1, 3, 1, 0), (0, 1, 3, 2, 0), (0, 1, 4, 1, 0), (0, 1, 4, 3, 0)
Z_6	(0, 4, 5, 2, 1, 3), (0, 1, 3, 0, 4, 3), (0, 1, 3, 0, 5, 3), (0, 1, 3, 1, 4, 3), (0, 1, 3, 1, 0, 3),
	(0, 1, 4, 0, 4, 3), (0, 1, 4, 0, 5, 3), (0, 1, 4, 2, 1, 3), (0, 1, 4, 2, 4, 3), (0, 1, 4, 3, 5, 3),
	(0, 1, 5, 1, 0, 3), (0, 1, 5, 2, 4, 3), (0, 1, 5, 2, 1, 3), (0, 1, 5, 4, 1, 3), (0, 1, 5, 4, 0, 3),
	(0, 1, 0, 2, 5, 3), (0, 1, 0, 3, 1, 3), (0, 1, 0, 3, 5, 3), (0, 1, 0, 4, 1, 3), (0, 2, 3, 0, 4, 3),
	(0, 2, 3, 1, 4, 3), (0, 2, 3, 1, 0, 3), (0, 2, 3, 2, 5, 3), (0, 2, 3, 2, 0, 3), (0, 2, 5, 0, 4, 3),
	(0, 2, 5, 3, 4, 3), (0, 2, 5, 3, 2, 3), (0, 2, 5, 4, 5, 3), (0, 2, 5, 4, 2, 3), (0, 2, 0, 3, 4, 3),
	(0, 2, 0, 1, 4, 3), (0, 2, 0, 5, 2, 3), (0, 2, 1, 2, 5, 3), (0, 2, 1, 2, 0, 3), (0, 2, 1, 4, 5, 3),
	(0, 2, 1, 4, 2, 3), (0, 2, 1, 5, 0, 3), (0, 2, 1, 5, 2, 3), (0, 3, 4, 0, 4, 3), (0, 3, 4, 0, 5, 3),
	(0, 3, 4, 2, 1, 3), (0, 3, 5, 0, 4, 3), (0, 3, 5, 0, 5, 3), (0, 3, 5, 4, 5, 3), (0, 3, 5, 4, 2, 3),
	(0, 1, 3, 2, 5, 3), (0, 1, 3, 2, 0, 3), (0, 1, 4, 3, 1, 3), (0, 2, 3, 0, 5, 3), (0, 2, 5, 0, 5, 3),
	(0, 2, 0, 3, 2, 3), (0, 3, 4, 2, 4, 3), (0, 1, 5, 1, 4, 3)
Z_7	(0, 1, 3, 6, 3, 1, 0), (0, 1, 3, 6, 3, 2, 0), (0, 1, 3, 6, 4, 1, 0), (0, 1, 3, 6, 4, 3, 0),
	(0, 1, 3, 6, 5, 3, 0), (0, 1, 3, 1, 5, 4, 0), (0, 1, 3, 1, 4, 3, 0), (0, 1, 3, 2, 5, 2, 0),
	(0, 1, 3, 2, 6, 2, 0), (0, 1, 3, 2, 6, 4, 0), (0, 1, 4, 6, 3, 1, 0), (0, 1, 4, 6, 3, 2, 0),
	(0, 1, 4, 6, 4, 1, 0), (0, 1, 4, 2, 4, 1, 0), (0, 1, 4, 2, 6, 5, 0), (0, 1, 4, 2, 6, 1, 0),
	(0, 1, 4, 2, 1, 5, 0), (0, 1, 4, 1, 3, 2, 0), (0, 1, 4, 1, 6, 5, 0), (0, 1, 4, 3, 5, 2, 0),
	(0, 1, 4, 3, 1, 3, 0), (0, 1, 4, 3, 1, 5, 0), (0, 1, 5, 1, 3, 2, 0), (0, 1, 5, 1, 6, 5, 0),
	(0, 1, 5, 3, 5, 4, 0), (0, 1, 5, 3, 6, 1, 0), (0, 1, 5, 3, 6, 5, 0), (0, 1, 5, 3, 2, 4, 0),
	(0, 1, 5, 4, 6, 2, 0), (0, 1, 5, 4, 6, 4, 0), (0, 1, 5, 4, 2, 4, 0), (0, 1, 5, 4, 2, 5, 0),
	(0, 1, 6, 2, 6, 1, 0), (0, 1, 6, 2, 6, 5, 0), (0, 1, 6, 2, 1, 5, 0), (0, 1, 6, 2, 1, 3, 0),
	(0, 1, 6, 3, 5, 4, 0), (0, 1, 6, 3, 6, 1, 0), (0, 1, 6, 3, 6, 5, 0), (0, 1, 6, 3, 2, 4, 0),
	(0, 1, 6, 5, 1, 3, 0), (0, 1, 6, 5, 1, 5, 0), (0, 1, 6, 5, 2, 4, 0), (0, 1, 6, 5, 2, 5, 0),
	(0, 1, 4, 6, 5, 3, 0), (0, 1, 4, 2, 4, 3, 0), (0, 1, 6, 1, 5, 4, 0), (0, 1, 6, 2, 4, 1, 0),
	(0, 1, 3, 6, 5, 2, 0), (0, 1, 3, 2, 5, 3, 0), (0, 1, 4, 6, 4, 3, 0), (0, 1, 4, 2, 1, 3, 0),
	(0, 1, 4, 3, 5, 3, 0), (0, 1, 5, 3, 5, 1, 0), (0, 1, 5, 3, 2, 5, 0), (0, 1, 6, 1, 4, 3, 0),
$^{@}Z_{8}$	(0, 1, 6, 3, 5, 1, 0), (0, 1, 6, 3, 2, 5, 0), (0, 1, 4, 6, 5, 2, 0), (0, 1, 6, 2, 4, 3, 0)
-28	(0, 1, 3, 6, 2, 7, 5, 4), (0, 1, 6, 5, 3, 7, 2, 4), (0, 1, 7, 2, 6, 3, 5, 4), (0, 2, 1, 5, 2, 6, 7, 4), (0, 2, 2, 6, 5, 1, 7, 4), (0, 2, 5, 1, 7, 6, 2, 4)
	(0, 2, 1, 5, 3, 6, 7, 4), (0, 2, 3, 6, 5, 1, 7, 4), (0, 2, 5, 1, 7, 6, 3, 4),
	(0, 1, 7, 3, 6, 5, 2, 4), (0, 2, 7, 6, 1, 5, 3, 4)

TABLE 3 List of directed 2-terraces with uniform 2-terraces from groups of order 3 to 8

[@]only uniform 2-terraces are mentioned to save space.

Terraces in bold denote uniform 2-terrace.

Group	a	b (any one)
Z_3	(0, 1)	(1, 0)
Z_4	(0, 3, 1)	(2,3,3), (0,0,1), (0,1,1), (1,1,2), (1,2,2), (2,2,3)
Z_5	(0, 1, 3)	(0,3,2), (1,4,3), (2,0,4), (3,1,0), (4,2,1), (0,4,2)
Z_6	(0, 2, 3, 1)	(0, 0, 3, 2), (0, 0, 5, 2), (1, 0, 0, 3), (1, 1, 0, 3), (2, 1, 1, 4), (2, 2, 1, 4),
		(3, 2, 2, 5), (4, 1, 0, 0), (4, 3, 3, 0), (5, 2, 1, 1), (3, 2, 5, 5), (5, 2, 2, 1)
Z_7	(0, 1, 6, 3)	(1, 3, 6, 5), (2, 4, 3, 6), (3, 6, 1, 0), (4, 0, 6, 1), (5, 4, 0, 2), (6, 5, 0, 3)
Z_8	(0, 1, 7, 4, 6)	(5, 1, 4, 4, 3), (0, 3, 2, 2, 6), (5, 1, 1, 4, 3), (3, 6, 5, 5, 1), (0, 0, 7, 3, 6),
		(3, 6, 6, 5, 1), (3, 3, 6, 2, 1), (3, 2, 6, 1, 1), (0, 3, 3, 7, 6), (5, 1, 0, 3, 3)
Z_9	(0, 1, 6, 4, 7)	(1, 0, 2, 8, 3), (2, 1, 3, 7, 4), (3, 2, 6, 8, 5), (4, 3, 0, 2, 6), (5, 0, 2, 8, 7),
		(6, 1, 3, 2, 8), (7, 2, 8, 1, 0), (8, 3, 2, 4, 1), (7, 4, 6, 1, 0), (6, 3, 5, 4, 8),
		(3, 0, 4, 6, 5), (2, 8, 7, 0, 4)

TABLE 4List of complementary pair of terraces from groups of order 3 to 9

	Table 5	
List of complementary trie	o of terraces from groups of order 4 to 8	

Group	a	b	c (any one)
Z_4	(0, 1)	(1, 0)	(0,2), (0,3), (2,1), (3,2)
Z_6	(0, 1, 3)	(0, 3, 1)	(0, 5, 5), (1, 0, 0), (2, 1, 1), (3, 2, 2), (4, 3, 3), (5, 4, 4),
			(1, 1, 0), (2, 2, 1), (3, 3, 2), (4, 4, 3), (5, 5, 4), (0, 0, 5)
Z_8	(0, 1, 3, 6)	(0, 4, 1, 1)	(0, 0, 7, 5), (0, 6, 5, 5), (0, 6, 6, 5), (0, 7, 5, 5), (0, 7, 7, 5),
			(1, 1, 7, 6)

References

- AFSARINEJAD, K. and HEDAYAT, A.S., Repeated measurements designs for a model with self and mixed carryover effects, Journal of Statistical Planning and Inference 106 (2002), pp. 449–459. MR1927725
- BAILEY, R.A., Quasi-complete Latin squares: Construction and randomization, Journal of the Royal Statistical Society B 46 (1984), pp. 323–334. MR0781893
- [3] BLAISDELL, E.A. and RAGHAVARAVO, D., Partially balanced change-over designs based on m-associate class PBIB designs, Journal of the Royal Statistical Society B 42 (1980), pp. 334–338. MR0596162
- [4] CARRIERE, K.C., Optimal two-period repeated measurement designs with two or more treatments, Biometrika 80 (1993), pp. 924–929. MR1282801
- [5] CHENG, C.S. and WU, C.F., Balanced repeated measurements designs, Annals of Statistics 8 (1980), pp. 1272–1283. MR0594644
- [6] COLLOMBIER, D. and MERCHERMEK, I., Optimal cross-over experimental designs, Sankhya: The Indian Journal of Statistics B 55 (1993), pp. 249– 261. MR1322035
- [7] DEY, A., GUPTA, V.K. and SINGH, M., Optimal change over designs, Sankhya: The Indian Journal of Statistics B 45 (1983), pp. 233–239.
 MR0748467
- [8] FLETCHER, D.J., A new class of change-over designs for factorial experiments, Biometrika 74 (1987), pp. 649–654. MR0909373
- [9] GILL, J.L., Design and Analysis of Experiments in the Animal and Medical Sciences, Vol II, Iowa State Univ. Press, Ames, 1978.

- [10] GRIZZLE, J.E., The two-period change-over design and its use in clinical trials, Biometrics 21 (1965), pp. 467–480.
- [11] HANFORD, K., Lecture Notes on Mixed Models, Spring, United States, 2005.
- [12] HEDAYAT, A.S. and AFSARINEJAD, K., Repeated measurements designs, I., In A Survey of Statistical Design and Linear Models (J.N. Srivastava, Ed.), pp. 229–242, North-Holland, Amsterdam, 1975. MR0375678
- [13] JONES, B. and KENWARD, M.G., Design and Analysis of Crossover Trials, Chapman and Hall/CRC, Boca Raton, 2003.
- [14] JONES, B. and DONEV, A.N., Modelling and design of cross-over trials, Statistics in Medicine 15 (1996), pp. 1435–1446.
- [15] KIEFER, J. and WYNN, H.P., Optimal balanced block and Latin squares designs for correlated observations, The Annals of Statistics 9 (1981), pp. 737–757. MR0624701
- [16] KUNERT, J., Optimality of balanced uniform repeated measurement designs, The Annals of Statistics 12 (1984), pp. 1006–1017. MR0751288
- [17] KUNERT, J., Crossover designs for two treatments and correlated errors, Biometrika 78 (1991), pp. 315–324. MR1131165
- [18] KUSHNER, H.B., Optimal repeated measurements designs: The linear optimality equations, The Annals of Statistics 25 (1997), pp. 2328–2344. MR1604457
- [19] MARTIN, R.J. and ECCLESTON, J.A., Variance-balanced change-over designs for dependent observations, Biometrika 85 (1998), pp. 883–892. MR1666707
- [20] MATTHEWS, J.N.S., Estimating dispersion parameters in the analysis of data from crossover trials, Biometrika 76 (1989), pp. 239–244.
- [21] MORGAN, J.P., Balanced polycross designs, Journal of the Royal Statistical Society B 50 (1988), pp. 93–104. MR0954735
- [22] NASON, M. and FOLLMANN, D., Design and analysis of crossover trials for absorbing binary endpoints, Biometrics 66 (2010), pp. 958–965. MR2758232
- [23] SENN, S., Cross-Over Trials in Clinical Research, John Wiley and Sons, New York, 1993.
- [24] TAKA, M.T. and ARMITAGE, P., Autoregressive models in clinical trials, Communications in Statistics: Theory and Methods 12 (1983), pp. 865–867.
- [25] VONESH, E.F. and CHINCHILLI, V.M., Linear and Nonlinear Models for the Analysis of Repeated Measurements, Marcel Dekker/CRC, New York, 1996. MR1633822
- [26] WILLIAMS, E.J., Experimental designs balanced for the estimation of residual effects of treatments, Australian Journal of Scientific Research 2 (1949), pp. 149–168. MR0033508