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Abstract: Crossover designs are often applied in Clinical trials, Agriculture field experiment, Nutrition experiment, etc. in which there is presence of residual effect of treatment in the current period of treatment application from preceding period of treatment application. In this paper, we reviewed some methods of construction of complete balanced crossover design for estimation of residual effects given by two authors William and Mausumi for both column and row approach either number of treatment V or N is even and odd the same results were obtained for both.

Keywords: Crossover design, residual effects, balanced design

Introduction

Crossover design is an experimental design in which experimental units are exposed to a sequence of different treatments over several periods. The usefulness of these designs have been found in the areas of clinical trials, nutrition experiment and agriculture field experiments. These designs produce direct effect and residual effect Sharma *et al.* (2007).

Many authors have introduced methods of construction for crossover design Grizzle (1965), Brown (1980), Grieve (1985), and; Andrew and Joseph (1986) address the issue of carryover effect in a situation of two period crossover trials. William (1949) gave method of construction of balanced crossover design for more than two treatments.

Mausumi (2002) and Durso (1984) developed the method of construction of counterbalancing for immediate sequential effects crossover designs. Hedayat and Minyang (2003) gave method of construction of balanced uniform crossover designs; and universal optimality for selected crossover designs.

KanchanChowdhury (2013) constructed an incomplete block change-over design balanced for first and second order residual effect, Mithilesh and Archana (2015) developed universally optimal balanced crossover design of first order residual effects and Mausumi and Alope (2013) present a review of major result in the construction of crossover design. For construction, if the number of treatment is even, a suitable cyclic Latin square is required; if the number of treatment is odd, two cyclic Latin square are required for design in order that the number of replicates must be a multiple number of treatments given by William and Gertrude (1957).

1. Need and conditions for balanced crossover designs

The needs for these designs are as follows:

- (i) To determine the effects of different sequences of treatment application.
- (ii) To discover whether or not a trend can be among the responses obtained by successive applications several treatments on a single experimental unit
- (iii) Experimental units are scarce and have to be used repeatedly
- (iv) The nature of experiment is such that it calls for special training over a long period of time.

Conditions for balanced CODs

- (i) Each treatment symbol occurs in a given sequence once
- (ii) Each treatment symbol occurs in a given period the same number of times.

- (iii) Every two treatment symbols appear together in the same number of sequences
- (iv) Every two treatment symbols follow each other should occur equally often in the sequences

2. Construction

We now review methods of constructions of balanced CODs

Method of construction of balanced CODs for more than two treatments column method

For constructing a balanced CODs for v treatment in v sequences and v periods where v is even number William (1949)

For sequence 1, treatment will be;

- (i) $1, 2, \dots, V/2$ occur in the periods $1, 3, \dots, V-1$ respectively
- (ii) $V/2 + 1, V/2 + 2, \dots, V$ occur in the periods $V, V-2, \dots, 2$ respectively
- (iii) the assignments for sequences $2, 3, \dots, V$ are obtained through a cyclic development of the arrangement sequence 1

For $V = 4$

Sequences

Period	1	2	3	4
1	1	2	3	0
2	0	1	2	3
3	2	3	0	1
4	3	0	1	2

For number of v is odd,

for sequence 1 the treatment will be

- (i) $1, 2, \dots, (V+1)/2$ occur in periods $1, 3, \dots, v$ respectively
- (ii) $(V+1)/2 + 1, (V+1)/2 + 2, \dots, V$ occur in periods $V-1, V-3, \dots, 2$ respectively
- (iii) The assignment for sequences $2, 3, \dots, V$ are obtained through a cyclic development of the arrangement for sequence 1
- (iv) The arrangement for sequence $(V+1)$ is the mirror image sequence V

For $V=5$

Sequences

Period	1	2	3	4	5	6	7	8	9	10
1	1	2	3	4	0	2	3	4	0	1
2	0	1	2	3	4	3	4	0	1	2
3	2	3	4	0	1	1	2	3	4	0
4	4	0	1	2	3	4	0	1	2	3
5	3	4	0	1	2	0	1	2	3	4

Methods of construction of balanced CODs for more than two treatments row method

For number of treatments v is even; for period 1 treatment will be;

- (i) 0, 1, V-1, 2, V-2, 3, V-3, ..., V/2
- (ii) the assignment for period 2, ..., V are obtained through a cyclic development of the arrangement for period 1

For V=6

Sequences

Period	1	2	3	4	5	6
1	0	1	5	2	4	3
2	1	2	0	3	5	4
3	2	3	1	4	0	5
4	3	4	2	5	1	0
5	4	5	3	0	2	1
6	5	0	4	1	3	2

For number of treatments v is odd; for period 1 treatment will be;

- (i) 0,1,V-1, 2,V-2, ..., (V-1)/2, (V+1)/2
- (ii) the assignment for period 2, ..., V are obtained through cyclic development of the arrangement for period 1
- (iii) reverse treatments in period 1 in the period (v+10 to obtain 2v rows

For V=3

Sequences

Period	1	2	3
1	0	1	2
2	1	2	0
3	2	0	1
4	2	1	0
5	0	2	1
6	1	0	2

Method of construction of counterbalancing for immediate sequential effects CODs

This method was discussed by Mausumi (2002), the procedure for the construction for number of treatment v is even and odd for sequence 1 and period 1 in both column and row method respectively is as follow as

- (i) 1,2,N, 3, N-1,4,N-2,...
- (ii) the subsequent sequences and period are obtained through cyclic development

Column Approach

N=4

Period	1	2	3	4
1	1	2	3	0
2	2	3	0	1
3	0	1	2	3
4	3	0	1	2

N=5

Sequences

Period	1	2	3	4	5	6	7	8	9	10
1	1	2	3	4	0	3	4	0	1	2
2	2	3	4	0	1	2	3	4	0	1
3	0	1	2	3	4	4	0	1	2	3
4	3	4	0	1	2	1	2	3	4	0
5	4	0	1	2	3	0	1	2	3	4

Row Approach

N=4

Sequences

Period	1	2	3	4
1	1	2	0	3
2	2	3	1	0
3	3	0	2	1
4	0	1	3	2

N=5

Sequences

Period	1	2	3	4	5
1	1	2	0	3	4
2	2	3	1	4	0
3	3	4	2	0	1
4	4	0	3	1	2
5	0	1	4	2	3
6	4	3	0	2	1
7	0	4	1	3	2
8	1	0	2	4	3
9	2	1	3	0	4
10	3	2	4	1	0

Model

$$Y_{hijk} = \mu + \alpha_h + \beta_k + \gamma_i + \delta_j + \epsilon_{hijk}$$

Y_{hijk} is the observation from the k^{th} experimental unit in the h^{th} period

μ is the general mean

α_h is the effect of the h^{th} period

β_k is the effect of the k^{th} unit

γ_i is the direct effect of treatment i

δ_j is the residual effect of the treatment j

ϵ_{hijk} is the random error

Source of variation(sv)	Degree of freedom(df)	Sum of squares(ss)	Mean square(ms)
Subject(Sequence)	mn-1	$\frac{\sum_{i=1}^{mn} Y_{i...}^2}{n} - \frac{Y_{...}^2}{mn^2}$	$\frac{SS_{Subject}}{mn-1}$
Treatment	n-1	$\frac{\sum_{j=1}^n \overline{Y_{.j}}^2}{n} - \frac{Y_{...}^2}{mn^2}$	$\frac{SS_{Treatment}}{n-1}$ $\frac{MS_{Treatment}}{MS_{Error}}$
Period	m(n-1)	$\frac{\sum_{k=1}^n Y_{..k}^2}{n} - \frac{Y_{...}^2}{mn^2}$	$\frac{SS_{Period}}{m(n-1)}$
Residual	n-1	$\frac{\sum_{q=1}^n R^2}{mn^3(n^2-n-2)}$	$\frac{SS_{Residual}}{n-1}$ $\frac{MS_{Residual}}{MS_{Error}}$
Error	(n-1)(mn-m-2)	By Subtraction	$\frac{SS_{Error}}{(n-1)(mn-m-2)}$
Total	mn ² - 1	$\sum_i^{mn} \sum_j^n \sum_k^n \sum_q^n Y_{ijkq}^2 - \frac{Y_{...}^2}{mn^2}$	

Result and Discussion

For methods of construction given by William(1949) column method approach for the number of treatment is even V=4 each treatment is preceded by each other treatment once and each treatment is preceded by each other treatment twice for treatment is odd V= 5. For row method approach for the number of treatment is even V=6 each treatment is preceded equally often in the design by each of the other treatments (V-1) times and; also each treatment is preceded by each other treatment an unequal number of times and one of the treatments preceded itself once for the number of treatment is odd V=3.

For methods of construction of counterbalancing for immediate sequential effects discussed by Mausumi (2002), column method approach for the number of treatment is even N=4 each treatment is preceded by each other treatment once and for the number of treatment is odd N=5 each treatment is preceded by each other treatment twice. For row method approach for the number of treatment is even N=4 each treatment is preceded equally often in the design by each of the other treatments (N-1) times and; also each treatment is preceded by each other treatment an unequal number of times and one of the treatments preceded itself once for the number of treatment is odd N=5.

It was discover that methods of construction given by William (1949) for column method for number of treatment v is even, the number of sequences are equal to number of periods and the number sequences double number of periods in order that the number of replicates must be a multiple number of treatments and the arrangement for sequence (V+1) is the reverse order of the arrangement for subject v for number of

treatment v is odd. For row method approach for the number of treatment v is even, the number of sequences are equal to number of periods and the number period double number of sequences in order that the number of replicates must be a multiple number of treatments and the arrangement for period (v+1) is the reverse order of period 1 for number of treatment v is odd.

Method of construction of counterbalancing for immediate sequential effects discussed by Mausumi (2002) for both column and row approach for the number of treatment is even and odd give the same result with above methods of construction given by William (1949) but used the same method of construction for both column and row approach either the number of treatment N is even or odd

Conclusion

We therefore conclude that using any of the methods given by these two authors William and Mausumi for both column and row approach either number of treatment V or N is even and odd, the same result shall be obtained and crossover designs are used for the purpose of residual effects.

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