CONSTRUCTION OF BALANCED INCOMPLETE SEQUENCE CROSSOVER DESIGNS FOR FIRST ORDER RESIDUAL EFFECT

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A Thesis submitted to the Department of Statistics, Faculty of Physical Sciences, University of Ilorin, Ilorin in partial fulfillment of the Requirements for the Award of the Degree of Doctor of Philosophy in Statistics.

APRIL, 2021

CERTIFICATION

This is to certify that this thesis is an original work carried out by Lanre ADEBARA with Matriculation Number 98/55EG079 in the Department of Statistics, Faculty of Physical Sciences, University of Ilorin. The thesis has been read and approved as meeting the requirements for the Award of Doctor of Philosophy in Statistics of the University of Ilorin, Ilorin, Nigeria.

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DEDICATION

To all my teachers.

ACKNOWLEDGEMENTS

I am most grateful to God Almighty for His mercy and goodness in my life. The only one common in my life, my all in all, my comforter and my defense. He has guided me from grass to grace, the qualifier of the unqualified.

My profound gratitude goes to my loving supervisor, Prof. B.L. Adeleke for his fatherly advice, assistance, intellectual stimulation, valuable suggestions, guidance and encouragement towards me.

I am grateful to the Head of Department. Prof. A.O. Adejumo for his words of encouragement during the course of this programme. My appreciation goes to other lecturers in the Department of Statistics, University of Ilorin especially, Professors B.A. Oyejola, E.T. Jolayemi, P.A. Osanaiye, , R.A. Ipinyomi, A.A. Adewara, W.B. Yahya & G.M. Oyeyemi, as well as Drs. A.O.Abidoye, A.A. Abiodun, , O. Job, M. K.Garba, I. Oloyede, , N.A. Ikoba, R.B. Afolayan, J. Popoola , O.R. Olaniran, I.V. Omekam, A.W. Banjoko, I.O Adeniyi & I. B. Amusa for their contributions.

I appreciate my darling wife Mrs. A.F. Adebara and my children Adebara Praise, Adebara Godwin and Adebara Precious for their immeasurable support, more so my profound gratitude goes to my cousin Mr T.O. Tinuoye for his moral and various supports.

I also wish to express my appreciation to my friends Dr O.S Obafemi, Dr. I.O. Ajao, Mr K.O. Adetunji, Mr Mohammed, Mr Abdulraham, Mr Odetunde and my appreciations also go to the entire academic staff of the Department of Mathematics and Statistics, Federal Polytechnic Ado- Ekiti for their understanding and encouragement.

L. Adebara

April, 2021

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ABSTRACT

Crossover design is a repeated measurements design in which individual subjects receives different sequences of treatments (t) during the different time period one at a time with object of studying differences between individual treatments. It has been found useful in several fields of research, among which are clinical trials and nutrition experiments involving dairy cattle .A noticeable feature of crossover design is that it leaves direct and carryover effects which is the effect of a treatment from previous time period on the response at the current time period in the succeeding periods. A design method that can generate designs for a large number of treatments is a challenge to researchers. Therefore, the aim of this study is to obtain method of construction of designs for a greater number of treatments. The objectives of this study were to: (i) determine prime numbers that satisfy primitive roots, $x = 2$ and 3 ; (ii) modify a construction method for balanced incomplete sequence crossover design for prime numbers for primitive root $x = 2$; (iii) construct a new class of balanced incomplete sequence crossover design for primitive roots $x = 2$ and 3; and (iv) use data set to validate the modified construction method.

A universally optimal Balanced Incomplete Sequence Crossover Design (BISCOD) for first order residual effect with parameter n (experimental units), t (number of treatments) and k (number of treatment in each experimental units or number of periods) was constructed in this study. This is to enhance the estimation of residual effect over class of design in which no treatment was allocated more than once on each subject, equal replications for all treatments in the first p-1 period and each treatment preceded each other treatment (k-1) times. A method of design that satisfies primitive root $x = 2$ and a proposed method that satisfies primitive roots x = 2 and 3 were obtained through balanced incomplete block design.

The findings of the study were that:

i. prime numbers that satisfied primitive roots $x = 2$ and 3 included 5, 7,11, 13,17, 19, 37, 61
ii. design using a modified construction method were generated for all prime number of treatments for primitive root x = 2;
iii. a construction method generates all prime number of treatments that satisfied primitive roots x = 2 and 3 was developed; and
iv. modified design construction method was validated

The study concluded that the modified method performed better in terms of generated designs for a greater number of treatments than existing method. The set of data from experiment of the crossover type was validated. The study recommended that the modified construction generated be used for prime numbers that satisfy primitive roots x = 2 and 3

CHAPTER ONE

GENERAL INTRODUCTION

1.0 Introduction

Crossover design is an experimental design for individual subject to receive different treatment sequences at different period one at a time with object of studying differences between individual treatments. This design is also known as change- over design, it been found useful in several fields of research, among which are clinical trials, nutrition experiments and pharmaceutical investigations.

Noticeable characterized is that it leaves direct and residual effects (the treatment effect from a period on the next immediate period response) in the immediate next periods (Sharma et al, 2007). To effectively eliminate residual effect, a common practice is to separate any two periods of treatment by an interval of time long called washout period. Balanced Incomplete Sequence Crossover Design for First Order Residual Effect shall be constructed later in this study.

The utility of this design come to the fore, when it is of interest to:

i. determine treatment effects of different sequences applications.

ii. study whether or not a trend is traced among the responses obtained by successive applications of several treatments on a single experimental unit and

iii. use a particular experimental unit repeatedly

Conditions for crossover design by Patterson (1952) are as follow

i. each treatment symbol must occur once in a given sequence.

ii. each treatment symbol occurs equally in a given period.

iii. treatment symbols which are pair occur together an equal number of sequences by removing the final period.

Crossover designs application in agriculture and clinical Experiments are given. A Latin square with rows representing period and columns representing subject (sequence) is crossover design type.

Example1: Agricultural experiment of testing effect of four different fertilizers A, B, C and Don the yield of wheat with sixteen similar plots as shown in Table 1.0.1

Table 1.0 .1: Crossover Design for 4 treatments

A	B	C	D
B	D	A	C
C	A	D	B
D	C	B	A

Note that in Table 1.0.1, each fertilizer found once in both row and column. Overall, each fertilizer (treatment) preceded each other fertilizer (treatment) once.

A research study performed in human that are aimed at evaluating a medical intervention is termed clinical trial. To avoid bias through order of administration of treatment, crossover design is used.

Example 2: Crossover Design involve two patients with two drugs A and B. First patient is allocated drug A during period 1 followed by drug B during period 2 in sequence 1, second patient is allocated drug B during period 1 followed by drug A during period 2 in sequence 2. The design is as shown in Table 1.0.2

Table 1.0.2: Crossover Design for 2 treatments 2 periods

	Sequence	
Period	1	2
1	A	B
2	B	A

Each treatment preceded each other treatment once

Therefore in medical clinical trial, treatments is not expected to cure totally but improve conditions of any disease, Piantadosi (2005), Andrew and Joseph (1986).

The allocation of treatments to subjects for purpose of monitoring treatments effects is called experimental design. Experiments are of two types namely absolute (experiment in which only a treatment is used and response is obtained) and comparative (experiment in which two or more treatments compared and responses are obtained). In general an experiment involves the planning and collection of measurements or observations according to pre-arranged plan, the system under study is set up and controlled by the investigator and some of experimental design are Crossover Design, Latin Square Design, Balanced Incomplete Block Design and so on. Klaus and Oscar (1994).

Experimental design components consist of firstly; the treatment design that tells which treatments should we choose and how many?, secondly; sampling design to determine at which observation are being taken and thirdly; the error control design which shows the actual treatment arrangement. The design of an experiment involves basically selection of treatments to be included in the experiment, specification of units (plots) to which treatments are to be applied, rules by which treatments are to be allocated to plots, measurement or other useful information obtained from each plot.

In general a good design will have the following characteristics, Alabi (2001).

i fairness to each treatment, that is, equal conditions as much as possible

ii grouping (plots within a group are more alike than plots in different group).

iii estimate of experimental error should be precisely made

Experimental design has three basic principles discussed by Angela and Daniel (1999) which are: Randomization (allocation of treatments to units with equal probability); Replication (repetition of a treatment in an experiment); Blocking (grouping of similar units together)

Prescott et al (1994), Angela and Daniel (1999) and Gupta et al (2015) discussed *balanced incomplete block design* with parameters t, b, r, k, λ of t treatment (entity which is studied), b blocks (experimental units which are similar), r replicate (number of times a treatment is allocated to experimental units), k block size (number of treatments in a block of experiment), *and* λ (number of times a pair of treatments occur together)

Latin square is type of row-column design with a great usefulness in experimental work and has many applications in statistical investigation.

Klaus and Oscar (1994) gave example of design of Latin square for an agricultural experiment in yield of crops through application of fertilizer with equal number of treatment, row and column for comparison. Latin letters are used for treatment symbol and one of its limitation is that numbers of rows, columns and treatments are the same.

Example 3: Design of Latin Square for 5 treatments

Five different grades of plastic materials A, B C, D, and E are tested to find whether they show any differences in surface smoothness after machine worked. Five machines and five operators are used for test and five samples of each plastic are tested and the operators and machines are distributed among the grades so that one operator, one machine and one grade are only associated once. The arrangement is as shown in Table 1.0.3

Table 1.0.3 : Design of Latin Square for 5 treatments

A	B	C	D	E
C	A	D	E	B
E	C	B	A	D
B	D	E	C	A
D	E	A	B	C

Note that in Table 1.0.3, each grade of plastic material found once in both row and column and preceded each other unequal numbers of time.

1.1 Classes of Design of Latin squares

In this section we shall consider three classes Orthogonal , Cyclic, and Standard and Semi-Standard Latin squares.

1.1.1 Orthogonal Latin Square

Two square which are of the same order super imposed on one another, every ordered pair of symbols occurs exactly once, the two are called orthogonal. If Latin letters represents one latin square and Greek letters represent the other one, the pair of such orthogonal is Graeco- Latin square.

Example 4: Orthogonal Latin Square of for 4 treatments

A B C D	A B C D	A B C D
B A D C	C D A B	D C B A
C D A B	D C B A	B A D C
D C B A	B A D C	C D A B

Example 5: Graeco-Latin squares for two sets of 4 treatments

$A\alpha$	$B\beta$	$C\gamma$	$D\delta$
$B\delta$	$A\gamma$	$D\beta$	$C\alpha$
$C\beta$	$D\alpha$	$A\delta$	$B\gamma$
$D\beta$	$C\delta$	$B\alpha$	$A\beta$

1.1.2 Standard and Semi-Standard Design of Latin Squares

Standard Latin square is when the first row and first column symbols follow natural order. Semi- Standard Latin square is when only the first row follow natural order.

Table 1.1.1 : Standard Latin Square for 4 treatment

A	B	C	D
B	A	D	C
C	D	B	A
D	C	A	B

Table 1.1.2: Semi-Standard Latin Square for 4 treatment

A	B	C	D
B	C	D	A
D	A	B	C
C	D	A	B

1.1.3 Cyclic Latin Square Design

A Latin square obtain from an initial row or column with subsequent rows or columns come through addition of one mode t is called cyclic Latin square

Table 1.1.3: Cyclic Latin Square for 4 treatments

1	2	3	0
2	3	0	1
3	0	1	2
0	1	2	3

Table 1.1.4: Cyclic Latin Square for 5 treatments

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

Furthermore, designs in this thesis exploited semi-standard latin square.

This cyclic design utilised an initial block say B = $\{i_1, i_2, \ldots, i_k\}$, while the other blocks of design are obtain by cyclic development which are expressed as B+1, B+2,…,B+(t-1). Infact the other blocks are through addition of 1 to initial block to obtain column two, add 2 to initial block to obtain column three up to addition of (t-1) to initial block to obtain column t. The addition operation in the foregoing cyclic development is implemented using arithmetic modulus v (see for example David and Wolock (1965)).

Illustration for seven treatments with initial block (1, 2, 4) is presented in example 7 below

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

1.2 Statement of the Problem

Different methods of constructing balanced incomplete sequence crossover design (BISCOD) were given by several authors, such as Sonawane (2009), Mithilesh and Archana (2015) and so on. The limitation of existing designs construction method given by Mithilesh and Archana (2015) was its inability to generate some prime numbers of treatments that satisfy primitive root x=2 using parameters from BIBD at $m \geq 1(1, 2, 3,\ldots)$ and different values of m in the two initial blocks sequences, m=0.5, 1, 1.5,… was addressed with the target of obtaining a solution that resulted in a modified method that generates such prime numbers of treatments.

1.3 Motivation for the study

It is well known that different construction methods of “BISCOD” have been developed. Mithilesh and Archana (2015) developed a new method of “BISCOD” for residual effects of first order in which each other treatment is being preceded by each treatment once. In this research work, our interest is to come up with a modified method of constructing “BISCOD” for first order residual effect.

1.4 Aim and Objectives of the Study

The aim of the study is to modify Mithilesh and Archana (2015) Balanced Incomplete Sequence Crossover Design (BISCOD) construction method for residual effects of first order for prime numbers of treatments. The specific objectives of the study were to:

(i) determine prime numbers that satisfy primitive roots x=2 and 3;

(ii) modify a construction method for BISCOD for prime number for primitive root x= 2 ;

(iii) construct a new class of BISCOD for primitive roots $x = 2$ and 3; and

(iv) validate the modified design construction method using information matrix

1.5 Significance of the Study

The focus of this study is on the construction of "BISCOD" for residual effects of first order, to take care of the limitation of Mithilesh and Archana (2015) design construction method. This research is necessary for a number of treatments with limited experimenter subjects which make each experimenter to be used repeatedly and also because of direct effect and residual effect (treatment effect from previous period on the response at the current period). The modified design construction method generated prime numbers of treatments which existing was unable to generate. Pharmacist, Clinical trial Physicians are the beneficiaries of this design.

1.6 Scope of the Study

The scope of this study is on the construction of balanced incomplete crossover designs for first order residual effect which says treatment effect will persist to only one period after period of treatment application.

1.7 Limitation of the Study

The limitation of this study was that modified design construction method with the two initial blocks sequences cannot generate non-zero elements of prime numbers of treatments at $m < 2$

1.8 Definition of Terms and Description

Subject

This is an experimental unit assigned twice or more to an identical or different treatment, Mausumi and Aloke, (2009). For example if a diet is for birds in one cage and another diet in another cage, then the cage is subject.

Period

This is an experimental unit's time in which treatments are allocated, Mausumi and Aloke, (2009). If one treatment in one minute or hour and another treatment is allocated another minute or hour, then minute or hour is what is called period.

Treatment

A treatment is an object that researcher administer to subject for study, Angela and Daniel (1999). For example different fertilizers applied to experimental units are treatments.

Residual Effect

A residual effect is the treatment effect from a period on the next immediate period response, Angela and Daniel (1999). If treatment effect of A persist to period where treatment B is allocated such effect is called residual effect.

Direct Effect

It is effect of a treatment which occur in the period of its allocation, Mausumi and Aloke (2009)

Latin Square

This is a design of square size t in which each treatment symbol occurs once in both row and once column respectively, Angela and Daniel (1999). Treatments A, B, C and D occur once in row and column.

Cyclic Latin Square

A Latin square obtain from an initial row or column with subsequent rows or columns come through addition of one mode t, Angela and Daniel (1999). If treatment 1, 2, 3 and 4 are in row one; row two treatments will be 2, 3, 4 and 5.

Primitive Root

A non-zero element of multiplicative group which generate others non-zero elements is called primitive root, Heath-Brown (1986). For instant 2 is non-zero elements that generates other non-zero elements 1, 3, 4, of prime number 5.

Sequence

A particular order in which related object follow each other. That is, pattern in which treatment are allocated into the unit.

Balanced Design

A design in which other treatment is being preceded equally by each treatment, Douglas (2001) is called a Balanced Design. Therefore if treatment A precedes treatment D four times, other treatment will precede each other four times.

Incomplete Balanced Design

If a treatment is never preceded by itself then design is incomplete balanced, Douglas (2001).

Balanced Incomplete Block Design

If occurrence of all the treatments is impossible in each block and every two treatments occur together in an equal number of times, Douglas (2001). For instant, a design of three treatments of block size two.

Uniform on the Period

A design is uniform on the periods, if all treatments have equal unit numbers on the period, Mausumi and Aloke (2009).

Uniform on the Subject

A design is uniform on the subject, if all treatments appear with period numbers on the subject, Mausumi and Aloke (2009).

Uniform Design

A design is refers to as uniform if it performs uniformity on both the periods and subjects, Mausumi and Aloke, (2009).

Washout Period

A space between time of allocation of one treatment to other into different periods to allow residual effect dried out, Angela and Daniel (1999).

Integer:

It is any number that is neither decimal number nor a fraction, Heath-Brown (1986).

Galois Field

It is a set on which the operations of multiplication, additions, substraction and division are defined and satisfy certain basic rules**,** Heath-Brown, (1986).

Algorithm

A sequence of steps which is carried out for a required output from a certain given input, Mithilesh and Archana (2015).

CHAPTER TWO

REVIEW OF RELATED LITERATURE

2.0 Introduction

This chapter is on the review of works that have been done by several authors and their contributions.

Crossover designs deal with direct and residual effects which have been found useful in several field of research. Construction method and applications of the designs had been discussed extensively by several authors. Cochran (1939), discussed experiments of given the manurial treatments on the different plots covered by a variety of combinations of nitrogenous and mineral fertilizers. Each plot received the same manurial treatment every year with the objective of the experiments was to determine which of the chemical constituents of the fertilizers were essential to the growth of the crop.

Jones and Kenward (2003) described crossover designs application in animal feeding trials of which two treatments have compared using two groups of cattle, the animals in one group received the treatments in the order ABAB and the animals in the other group received the treatments in the order BABA based on the number of periods.

Stephen (2002), Hinkelmann and Kempthorne (2005), discussed usefulness of this design in clinical trials and pharmaceutical studies. Patients were given a number of treatments, that is, two treatments X and Y were compared. Patients were given either X or Y in the first period and crossed over to the other treatment with purpose of studying the difference in the effects of treatment. Patient who failed to response or suffered a replase would then be given alternative therapies and so on.

Miekel (1974) usefulness of the designs in weather modification experiment in which the sum of squared rank test is a valuable tool for evaluating certain weather modification experiment. This test is applicable to an experimental design in which treatment such as seeding or not seeding clouds with similar silver iodide are randomly applied to a specific target vicinity.

Schilich (1993) and Kunert (1998) discussed sensory and consumer studies where assessors in sensory experiment are subjected to a series of treatments, that is, products and their assessment of each treatment are recorded and also affects the behavior of assessors if he or she takes product more than once.

Namboodiri (1972), Chow and Liu (1992) and Durier et al (1997) discussed bio-equivalence studies for psychology. It is applicable when it is known that differences are large and may obscure treatment effects with examples in the area of human psychophysiology. Large individual differences may obscure treatment effects unless they are adequately accounted for.

Cochran and Cox (1957) gave an experiment on three treatments - three periods of allocating fertilizer to different plots, where it was shown that for balanced design, for odd numbers of treatments, two cyclic Latin design was used. The design is as shown in Table 2.0.1

Table 2.0.1 : Design of Crossover for 3-treatments, 3-periods

	Sequence					
Period	1	2	3	4	5	6
1	A	B	C	A	B	C
2	C	A	B	B	C	A
3	B	C	A	C	A	B

Each treatment preceded each other treatment twice

2.1 Construction of Two Treatments--Two Periods Crossover Design

Grizzle (1965), Varma and Chiltin (1974), Walleristein and Fisher (1977), Layard and Arvesen (1978), Hill and Armitage (1979), Brown (1980), Grieve (1985),Castelian and Patel (1985), Andrew and Joseph (1986), discussed construction methods for two treatments and address the situation of residual effect. In this situation subject 1 receives treatments sequence A-B for period 1 and period 2 respectively; subject 2 receives treatments sequence B-A in reverse order. The design is as shown in Table 2.1.1

Table 2.1.1 : Design of Crossover for 2-treatments, 2-periods

	Subject	
Period	I	II
I	A	B
II	B	A

Each treatment preceded each other treatment once

2.2 Balanced Crossover Design for More than Two Treatments

Williams (1949) discussed construction method for more than two (2) treatments

2.2.1 Balanced Crossover Design using Column Method

Case 1 When the number of treatments, v is even, sequence 1 receives treatments as follows

(i) 1,2,…, $^t/_2$ occur in the periods 1,3,…, t-1 respectively

(ii) $^t/_2$ + 1, $^t/_2$ +2,…, v occur in the periods t, t-2,…, 2 respectively

(iii) the assignments for sequence 2,3,…,t are obtained through the arrangement for sequence 1 cyclically.

Table 2.2.1: Design of Crossover for 4-treatments, 4-periods

Period	Sequence I	II	III	IV
I	1	2	3	0
II	0	1	2	3
III	2	3	0	1
IV	3	0	1	2

Each other treatment is being preceded by each treatment once

Case 2 : For treatment number, t is odd, sequence 1 receives treatments as follows

(i) 1, 2,…$^{(t+1)}/_2$ occur in periods 1,3, …, t respectively

(ii) $^{(t+1)}/_2$ + 1,$^{(t+1)}/_2$ + 2,…,v occur in periods t-1, t-3,…,2 respectively

(iii) the assignment for subject 2, 3,…,tare obtained through the arrangement for sequence 1 cyclically

(iv) the arrangement for sequence (t+1) is reverse order of sequence t

Table 2.2.2: Design of Crossover for 5-treatments, 5-periods

Period	Sequence I	II	III	IV	V	VI	VII	VIII	IX	X
I	1	2	3	4	0	2	3	4	0	1
II	0	1	2	3	4	3	4	0	1	2
III	2	3	4	0	1	1	2	3	4	0
IV	4	0	1	2	3	4	0	1	2	3
V	3	4	0	1	2	0	1	2	3	4

Each other treatment is being preceded by each treatment twice

2.2.2 Balanced Crossover Design using Row Method

Case 1: For treatment number period 1 receives treatments as follows

(i) 0, 1, t-1, 2, t-2, 3, t-3, …, t/2

(ii) adding 1 to each element of the preceding period to obtain successive periods

Table 2.2.3: Design of Crossover for 4-treatments, 4-periods

	Sequence			
Period	I	II	III	IV
I	0	1	3	2
II	1	2	0	3
III	2	3	1	0
IV	3	0	2	1

Each other treatment is being preceded by each treatment (t-1) times

Case 2: For treatment number t is odd, period 1 receives treatments as follows

(i) 0, 1, t-1, 2, t-2, …

(ii) adding 1 to each element of the preceding period to obtain successive period

(ii) period 1 is reversed in period (t+1) to obtain 2t periods

The design is as shown in Table 2.2.4

Table 2.2.4: Design of Crossover for 5-treatments, 10-periods

	Sequence				
Period	I	II	III	IV	V
I	0	1	4	2	3
II	1	2	0	3	4
III	2	3	1	4	0
IV	3	4	2	0	1
V	4	0	3	1	2
VI	3	2	4	1	0
VII	4	3	0	2	1
VIII	0	4	1	3	2
IX	1	0	2	4	3
X	2	1	3	0	4

Each other is being preceded by each treatment an unequal number of times and one of the treatments preceded itself once

2.3 Strongly Balanced Uniform Crossover Designs

Berenblut (1964), Keifer (1975); and Cheng and Wu (1980) described construction method in which treatment number t is odd and even. For treatment number t is even or odd, a (t, t^2, t) design exists, where t represents treatment number, t^2 represents unit number and 2t represents period number. The design is as shown in Table 2.3.1

Table 2.3.1: Design of Crossover for 3-treatments, 6-periods

Period	Sequence I	II	III	IV	V	VI	VII	VIII	IX
I	0	0	0	1	1	1	2	2	2
II	0	1	2	0	1	2	0	1	2
III	1	1	1	2	2	2	0	0	0
IV	1	2	0	1	2	0	1	2	0
V	2	2	2	0	0	0	1	1	1
VI	2	0	1	2	0	1	2	0	1

Each other treatment is being preceded by each treatment and itself (2t-1) times

2.3.1 Counterbalancing for Immediate Sequential Effects Crossover Design

Durso (1984) and Mausumi (2002) gave construction method which are the procedures of construction methods similar to that of Williams (1949) for even and odd number of treatment.

Case1: Column method for treatment number

Sequence 1 receives treatments as follows

(i) 1,2, t, 3, t-1,4,t-2,…

(ii) the subsequent sequences are obtained cyclically.

The design is as shown in Table 2.3.2

Table 2.3.2: Design of Crossover for 4-treatments, 4-periods

Period	I	II	III	IV
I	1	2	3	0
II	2	3	0	1
III	0	1	2	3
IV	3	0	1	2

Each other treatment is being preceded by each treatment once

Sequence v is reversed in sequence vi to obtain 2t sequences in the design shown in Table 2.3.3

Table 2.3.3: Design of Crossover for 5-treatments, 5-periods

	Sequences									
Period	I	II	III	IV	V	VI	VII	VIII	IX	X
I	1	2	3	4	0	3	4	0	1	2
II	2	3	4	0	1	2	3	4	0	1
III	0	1	2	3	4	4	0	1	2	3
IV	3	4	0	1	2	1	2	3	4	0
V	4	0	1	2	3	0	1	2	3	4

Each other treatment is being preceded by each other treatment twice

Case 2 Row method for treatment number, period 1 receives treatment as follows

(i) 1, 2, t, 3, t-1,4,t-2,…

(ii) the subsequent periods are obtained cyclically.

(iii) period 1 is reversed in period (t+1) to obtain 2t periods

The design is as shown in Table 2.3.4

Table 2.3.4: Design of Crossover for 5-treatments, 10-periods

Period	Sequences I	II	III	IV	V
I	1	2	0	3	4
II	2	3	1	4	0
III	3	4	2	0	1
IV	4	0	3	1	2
V	0	1	4	2	3
VI	4	3	0	2	1
VII	0	4	1	3	2
VIII	1	0	2	4	3
IX	2	1	3	0	4
X	3	2	4	1	0

Each treatment is being preceded by each treatment an unequal number of times and one of the treatments preceded itself once

Table 2.3.5: Design of Crossover for 4-treatments, 4-periods

Period	Sequences I	II	III	IV
I	1	2	0	3
II	2	3	1	0
III	3	0	2	1
IV	0	1	3	2

Each treatment is being preceded by each treatment (t-1) times

2.4 Construction of Balanced Uniform Crossover Designs

Hedayat and Min Yang (2003), presented construction method for an extra period design where last row in William (1949) designs was repeated to obtain p+1 period.

When the number of treatments, t is even, sequence 1 receives treatments as follows

(i) 1,2,…, $^t/_2$ occur in the periods 1,3,…, t-1 respectively

(ii) $^t/_2$ + 1, $^t/_2$ +2,…, v occur in the periods t, t-2,…, 2 respectively

(iii) the assignments for sequence 2,3,…,t are obtained through the arrangement for sequence 1 cyclically

(iv) repeat the last period to obtain p+1 period

The design is as shown in Table 2.4.1

Table 2.4.1: Crossover Design for 4-treatments, 5-periods

	Sequence			
Period	I	II	III	IV
I	1	2	3	0
II	0	1	2	3
III	2	3	0	1
IV	3	0	1	2
V	3	0	1	2

Each other treatment is being preceded by each treatment and itself once

Sequence v is reversed in sequence vi to obtain 2t sequences in the design shown in Table 2.4.2

Table 2.4.2: Design of Crossover for 5-treatments, 6-periods

	Sequence									
Period	I	II	III	IV	V	VI	VII	VIII	IX	V
I	1	2	3	4	0	2	3	4	0	1
II	0	1	2	3	4	3	4	0	1	2
III	2	3	4	0	1	1	2	3	4	0
IV	4	0	1	2	3	4	0	1	2	3
V	3	4	0	1	2	0	1	2	3	4
VI	3	4	0	1	2	0	1	2	3	4

Each other treatment is being preceded by each treatment and itself twice

2.5 Construction of Balanced Incomplete Sequence Crossover Designs

Bose (1939) discussed construction method with design parameters t=mk+1, b=m(mk+1),r=mk, λ =k-1 using initial blocks (x^{i} x^{i+m} x^{i+2m} …, $x^{i+(k-1)m}$) where x is a primitive root of Galois field and i ranges from 0 to m-1.

Sprott (1954) presented Bose’s construction method that shown period number less than treatment number for prime power.

Varghese and Sharma (2000) and Sonawane(2009) reviewed the work of Sprott (1954) with example of treatment number t is 7.The design can be constructed by developing mod t, for initial blocks:(x^{i}, x^{i+m}, x^{i+2m},…,$x^{i+(k-1)m}$) , i= 0,1,…,m-1; x is a primitive root and for making this design to be balanced, last period treatments are repeated in the pre-period(0).

The design is as shown in Table 2.5.1

Table 2.5.1: Crossover Design for 7-treatments, 3-periods

Sequence

Period	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV
0	4	5	6	0	1	2	3	5	6	0	1	2	3	4
I	1	2	3	4	5	6	0	3	4	5	6	0	1	2
II	2	3	4	5	6	0	1	6	0	1	2	3	4	5
III	4	5	6	0	1	2	3	5	6	0	1	2	3	4

Patterson and Lucas(1962) presented construction method for k treatments of BIBD that form a block of a balanced incomplete block design. Let the parameters of the considered BIB design be t,b,r,k, λ with b block arrange in b rows. The resultant design of BISCOD with parameters t,p,k,n=bk^2 r^1=rt is given in Table 2.5.2

Table 2.5.2: Arrangement of Parameters t=4, b=6, r=3, k=2 and λ =1 in b rows

1	2
1	3
1	4
2	3
2	4
3	4

Each arrangement of pair of treatments per row in Table 2.5.2 was allocated to four different sequences. The design is as shown in Table 2.5.3

Table 2.5.3: Design of Crossover for 4-treatments, 2-periods

Sequence

period	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
I	1	2	1	2	1	3	1	3	1	4	1	4
II	2	1	1	2	3	1	1	3	4	1	1	4

PERIOD	XIII	XIV	XV	XVI	XVII	XVIII	XIX	XX	XXI	XXII	XXIII	XXIV
I	2	3	2	3	2	4	2	4	3	4	3	4
II	3	2	2	3	4	2	2	4	4	3	3	4

Each other treatment is being preceded by each treatment and itself once

Table 2.5.4: Arrangement of Parameter t=3,b=3, r=2, k=2, λ =1 in b rows

1	2
2	3
3	1

Each arrangement of pair of treatments per row in Table 2.5.4 was allocated to four different sequences. The design is as shown in Table 2.5.5

Table 2.5.5: Design of Crossover for 3-treatments, 2-periods

	Sequence											
Period	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII
I	1	2	1	2	2	3	2	3	3	1	1	3
II	2	1	1	2	3	2	2	3	1	3	1	3

Each other treatment is being preceded by each treatment and itself once

2.6 Construction of Universally Optimal Balanced Crossover Designs

Hedayat and Afsarinejad (1978) presented Universally Optimal (UO) design estimation of both direct and residual effects for uniform designs classes. It was stated that if design is universally optimal, then it is D, A and E optimal but in some situations it is possible to identify the universally optimal design without actually computing trace for each design

Cheng and Wu (1980) discussed UO design for estimation of residual effect over designs classes in which n is subject, p is period and μ is block size

(i) n= μ_1t p= μ_2t for some integers μ_1 μ_2

(ii) no treatment appears twice on a subject

(iii) equally replication of treatments in the first p-1 periods.

Sadegh (1997) discussed method for a design where number of period equal number of treatment N subjects divided into g group with n_i (i=1,2,…,g) in each group such that N= $\sum_{i=1}^{g} ni$; i denotes group, j denotes subject within the group and k denotes period. A Reduced table for Group mean and Period mean that refers to as Gy

Table 2.6.1 : Reduced table of Group Mean x Period Mean

Group	Period 1 2 . . . p	Average in period
1	$\bar{y}_{11.}$ $\bar{y}_{1..}$ - - - $\bar{y}_{1p}$	$y_{1,..}$
2	$\bar{y}_{21.}$ $y_{22..}$ - - - $\bar{y}_{2p}$	$y_{2,,,}$
.	. - - - - - - - .	.
.	. - - - - - - - -	.
g	$\bar{y}_{g1.}$ $y_{22..}$ - - - $\bar{y}_{2p}$	$y_{g\ldots}$
Average in group	$y_{.1}$ $y_{.2}$ - - - $y_{.p}$	$y_{\ldots}$

Period mean $y_{.j} = (\sum n_i y_{ij}) / N$ Grand mean $y_{.j} = (\sum n_i y_{i.}) / N$

To identify where the treatment information resides, we give the following G matrix as the idempotent matrix which produces a vector Gy, where each value y_{ijk} in the original data vector is replaced by its group multiply by period mean.

Thus Gy has length Np and contains the ith group and jth period, each mean occurs n_i times

Hedayat and Yang (2004) discussed universally optimal (UO) for crossover designs selected when subject effects are fixed and representing a larger population of interest subject were less randomly selected.

Hedayat et al (2006) discussed how to obtain optimality for special case of crossover design when number of period, p less than number of treatment, t (Incomplete Sequence Crossover Design). It was stated that to identify optimal designs for Incomplete Sequence Crossover Designs, two large subclasses of these designs in the entire class $\Omega_{t, n, p}$ contributed by Kiefer (1975) was used. A design in $\Omega_{t, n, p}$, of which t denotes treatment, n denotes subject and p denotes period is Universally Optimal in a subclass of Ω if design belongs to the subclass.

The two subclasses are

(i) $\Omega^1 = \Omega^1_{t, n, p}$ which consisting of all designs in which each treatment is replicated n/t times in the last period.

(ii) $\Omega^2 = \Omega^2_{t, n, p}$, subclass of $\Omega_{t, n, p}$ consisting of all designs in which each treatment is replicated n/t times in the last period, no treatment is immediately preceded by itself in any of the treatment sequences of the design.

They made the contribution that a design of this special case is universally optimal and follow the A, D, and E optimality. A design that is universally optimal in $\Omega^1_{t, n, p}$ is also universally optimal in $\Omega^2_{t, n, p}$

Bose and Dey (2009), Kunert (1984), Raghavarao and Shah (1984), and Wei Zheng (2013)

Hedayat and Zheng (2010) presented design which is optimal and efficient for testing a subject effectis random for test control. When p=t=4 and n=16, it was shown that the design and subject dropout setup does not exist. A design which maximizes all realization of information matrix

$$d = \begin{matrix} 2 & 1 & 2 & 3 & 3 & 4 & 3 & 2 & 1 & 1 & 1 & 2 & 4 & 4 & 4 & 3 \\ 4 & 4 & 3 & 4 & 1 & 1 & 2 & 1 & 2 & 2 & 3 & 4 & 3 & 3 & 2 & 1 \\ 3 & 2 & 1 & 1 & 2 & 3 & 4 & 4 & 3 & 3 & 4 & 1 & 2 & 2 & 1 & 4 \\ 3 & 2 & 1 & 1 & 2 & 3 & 4 & 4 & 4 & 4 & 2 & 3 & 1 & 1 & 3 & 2 \end{matrix}$$

Zhao and Majumdar(2012) discussed uniformly balanced crossover designs is efficient under subject dropout.In many studies that involve human subjects, such as clinical trials, it is very common that subjects drop out of the study prior to the completion. Crossover designs are generally used for studies with a small number of periods, which implies that the number of periods after dropout will be small.

For the case t = 3 and n = 6, p=2 as treatments labeled as 0,1, 2, then design

0 1 2 1 2 0

1 2 0 0 1 2

Mithilesh and Archana (2015) presented construction method of BISCOD for residual effects of first order for selected treatments number that satisfy primitive root x=2 from BIBD parameter where m value for BIBD parameter is not the same with m values for the two initial block sequences which was reviewed by Adebara et al (2020).

For example, given the following parameter;

$t=4m+1$, $b= 2(4m+1)$, $r= 4m$, $k= 2m$, $\lambda = 2m-1$ for $m \geq 1$

For t=5, m=1, k=2, x=2 then a BIBD with the two initial block sequences exist

$I_1 = (x^0, x^2, x^4, \ldots, x^{4m-2})$, m= 0.5, 1, 1.5, … = 1,4

$I_2 = (x, x^3, x^5, \ldots, x^{4m-1})$, m= 0.5, 1, 1.5, … = 2,3

First initial block sequence multiply by every non-zero elements of Gf(5)=(1,2, 3,4) to obtain initial sequences with 4 terms with mod 5,

1 2 3 4

4 3 2 1

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters $t = 5$, $N = 20$, $k = 2$.

The modified design construction method that generated prime numbers of treatments that Mithilesh and Archana (2015) cannot generate was presented in chapter three.

CHAPTER THREE

METHODOLOGY

3.0 Introduction

This chapter is on the methodology used and design construction for both Mithilesh and Archana (2015) and Modified design constructions for BISCOD.

3.1 Construction of Balanced Incomplete Sequence Crossover Design for First Order Residual Effect

Let $t= 4m + 1$ be a prime number and let x be a primitive root of GF(t). Consider a BIBD with the parameters t=4m+1, b= 2(4m+1), r= 4m, k= 2m, λ = 2m-1, m $\geq$1positive integer (1,2,3,…,) and different values m which are real numbers were used to obtain non-zero elements of prime numbers of treatments from the two initial block sequences as shown in (3.1) and (3.2) Mithilesh and Archana (2015).

$I_1 = (x^0, x^2, x^4, . . ., x^{4m-2})$, m= 0.5, 1, 1.5, … (3.1)

$I_2 = (x, x^3, x^5, . . ., x^{4m-1})$, m= 0.5, 1, 1.5, … (3.2)

3.1.1 Construction Procedure for BISCOD

- Choose any initial block sequence between equations (3.1) and (3.2) from section 3.1
- Obtain the (t-1) initial sequences from the above block by multiplying with elements which are non-zero of GF(t)
- By developing the initial sequences mod (t), we get a balanced crossover design which is universally optimal (UOBCOD) for first order with parameter t= 4m+1, rt(n)=4m(4m+1), k= 2m

The method will be illustrated through examples 1 and 2

Example 1: For t=5, m=1, x=2, Then a BIBD with two initial blocks (1,4) and (2, 3) exist mod 5

Consider the first initial block (1,4) then four initial sequences will be

1	2	3	4
4	3	2	1

By developing the above 4 initial sequences mod 5, we get a UOBCOD for residual effects of first order with parameters t = 5, N = 20, k = 2

Example 2: For t =13,m=3, x=2 Then a BIBD with two initial blocks(1, 4, 3, 12, 9, 10) and (2, 8, 6, 11, 5, 7) exist mod 13

Consider the first initial block (1 4 3 12 9 10), then twelve initial sequences will be

1	2	3	4	5	6	7	8	9	10	11	12
4	8	12	3	7	11	2	6	10	1	5	9
3	6	9	12	2	5	8	11	1	4	7	10
12	11	10	9	8	7	6	5	4	3	2	1
9	5	1	10	6	2	11	7	3	12	8	4
10	7	4	1	11	8	5	2	12	9	6	3

By developing the above twelve initial sequences mod 13, we get a UOBCOD for residual effects of first order with parameters t = 13, N = 156, k = 6

3.2 Modified Balanced Incomplete Sequence Crossover Design for First Order Residual Effect

The modified design construction method for BISCOD for first order residual effect was presented, the BIBD parameters and the two initial blocks sequences are modified to generate prime number of treatment which Mithilesh and Archana (2015) were unable to generate. Parameters $k \geq 2$ (2, 3, 4,…,) and m=2 were introduced and the number of period used two (2) and the code in the appendix was used to generate non-zero elements of prime number of treatments in this study.

Universally optimal design is A- optimal, D- optimal and E- optimal. A design in the class of competing design D with information matrix C_d is universally optimal over design D if the following two conditions are satisfied

(i) the matrix C_d is symmetric

(ii) (ii) the trace of C_d is maximized connected to all other design in Design

3.2.1 Design Construction Method I

A modified design construction method for BISCOD that generates every elements which is non zero prime numbers that satisfy primitive root x=2 from BIBD with two initial blocks sequences are considered.

Consider the BIBD with parameters t=2k+1, b=2(2k+1), r = t-1, $p=k \geq 2$ (2, 3, 4,…,) , λ =k-1,

t is the number of treatments

b is the number of blocks

r is the replication,

k is block sizes

λ is occurrence of two treatment together in sequences

x is primitive root

Setting x^0 to be treatment 1 and $x^1 \equiv x$ for both initial blocks in equations (3.3) and (3.4) below respectively, $m= 2$, $p=k \geq 2$ (2,3,4,…,)

Therefore the two initial blocks sequences are:

$$I_1 = (x^0, x^m, x^{2m}, \ldots x^{2k-x}), m=2, \quad p = k \geq 2(2,3,4,\ldots,) \qquad (3.3)$$

$$I_2 = (x^1, x^{m+1}, x^{2m+1}, \ldots, x^{2k-x+1}), m=2, \quad p = k \geq 2 (2,3,4,\ldots,) \qquad (3.4)$$

3.2.1.1 Construction Procedure for Modified BISCOD

This construction procedure is for all cases of design construction methods in this study.

- Select any of the two blocks sequences in equations 3.3 and 3.4
- Multiplying the selected block with every element which is non-zero of GF(t) to obtain (t-1) initial sequences
- then a design of UOBCOD for first order residual effect with parameters $t=2k+1$, $n=2k(2k+1)$, $k \geq 2$ is constructed by developing the above (t-1) initial sequences

3.2.1.2 Construction of BISCOD when the number treatment is 5

For t=5, m=2, k=2, x=2 then a BIBD with the two initial blocks exists

$I_1 = (x^0, x^m, x^{2m}, \ldots x^{2k-x})$, $I_2 = (x^1, x^{m+1}, x^{2m+1}, \ldots, x^{2k-x+1})$ for m=2, k= 2, x=2

$I_1 = (x^0, x^m)$

$=(2^0, 2^2) = (1,4)$

In mod 5 = (1, 4)

$I_2 = (x^1, x^{m+1})$

$= (2^1, 2^{2+1})$

$= (2^1, 2^3) = (2, 8)$

In mod5= (2, 3)

Therefore the two initial blocks sequences are (1, 4) and (2, 3) in mod 5

Select first initial block sequence (1, 4)

Multiply the first initial block with every non-zero elements of Gf (5)=(0,1,2,3,4) to obtain initial sequences with 4 terms

1x1=1   1x2=2   1x3=3   1x4=4

4x1=4   4x2=8   4x3 12   4x4=16

In Mod5 the initial sequences are : (1 2 3 4) and

(4 3 2 1)

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 5, n = 20, k = 2.

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

From the above design each other treatment is being preceded by each treatment once

Select second initial block (2, 3)

Multiply the first initial block with every non-zero elements of Gf (5)=(0,1,2,3,4) to obtain initial sequences with 4 terms

2x1=2   2x2=4   2x3=6   2x4=8

3x1=3   3x2=6   3x3=9   3x4=12

In Mod5 the initial sequences are: (2 4 1 3) and

(3 1 4 2)

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 5, n = 20, k = 2.

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

From the above design each other treatment is being preceded by each treatment once

3.2.1.3 Construction of BISCOD when the number treatment is 11

For t=11, m=2,k=5, x=2 then a BIBD with the two initial blocks exists

$I_1 = (x^0, x^m, x^{2m}, \ldots x^{2k-x})$, $I_2 = (x^1, x^{m+1}, x^{2m+1}, \ldots, x^{2k-x+1})$ for m=2, k= 5, x=2

$I_1 = (x^0, x^m, x^{2m} ,x^{3m} , x^{4m})$
$=(2^0, 2^2, 2^4 , 2^6, 2^8)$

In Mod11 = (1, 4, 5, 9, 3)

$I_2 = (x^1, x^{m+1} , x^{2m+1} , x^{3m+1} , x^{4m+1})$
$= (2^1, 2^{2+1}, 2^{4+1}, 2^{6+1}, 2^{8+1})$
$= (2^1, 2^3\ 2^5\ 2^7\ 2^9)$

In Mod11= (2, 8, 10, 7, 6)

Therefore the two initial blocks sequences are: (1, 4, 5, 9, 3) and (2, 8, 10, 7, 6) in mod 11

Select first initial block sequence (1, 4, 5, 9, 3)

Multiply the first initial block with every non-zero elements of Gf (11)=(0,1,2,3,4,5,6,7,8,9,10)

to obtain initial sequences with 10 terms

1x1	1x2	1x3	1x4	1x5	1x6	1x7	1x8	1x9	1x10
4x1	4x2	4x3	4x4	4x5	4x6	4x7	4x8	4x9	4x10
5x1	5x2	5x3	5x4	5x5	5x6	5x7	5x8	5x9	5x10
9x1	9x2	9x3	9x4	9x5	9x6	9x7	9x8	9x9	9x10
3x1	3x2	3x3	3x4	3x5	3x6	3x7	3x8	3x9	3x10

We have

1	2	3	4	5	6	7	8	9	10
4	8	12	16	20	24	28	32	36	40
5	10	15	20	25	30	35	40	45	50
9	18	27	36	45	54	63	72	81	90
3	6	9	12	15	18	21	24	27	30

In Mod11the initial sequences are :

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

A universally optimal BISCOD is obtain cyclically for residual effects of first order with parameters t= 11, n = 110, k = 5.

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

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

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

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

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

From the above design each other treatment is being preceded by each treatment 4 times

select second initial block sequence (2, 8, 10, 7, 6)

Multiply the second initial block with every non-zero elements of Gf(11)=(0,1,2,3,4,5,6,7,8,9,10)

to obtain initial sequences with 10 terms

2x1	2x2	2x3	2x4	2x5	2x6	2x7	2x8	2x9	2x10
8x1	8x2	8x3	8x4	8x5	8x6	8x7	8x8	8x9	8x10
10x1	10x2	10x3	10x4	10x5	10x6	10x7	10x8	10x9	10x10
7x1	7x2	7x3	7x4	7x5	7x6	7x7	7x8	7x9	7x10
6x1	6x2	6x3	6x4	6x5	6x6	6x7	6x8	6x9	6x10

We have

2	4	6	8	10	12	14	16	18	20
8	16	24	32	40	48	56	64	72	80
10	20	30	40	50	60	70	80	90	100
7	14	21	28	35	42	49	56	63	70
6	12	18	24	30	36	42	48	54	60

In mod11 the initial sequences are :

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

A universally optimal BISCOD is obtain cyclically for residual effects of first order with parameters t= 11, n = 110, k = 5.

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

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

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

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

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

From the above design each other treatment is being preceded by each treatment 4 times

3.2.2 Design Construction Method II

A class of new construction method for BISCOD for residual effects of first order for prime number of treatments, that satisfies primitive root x= 2 and 3 from BIBD with two initial blocks sequences. This design construction method II is more efficient than design construction method I in that it generated every non-zero elements of prime numbers of treatments that satisfy both primitive roots x=2 and x=3.We shall follow the above construction procedure under modified construction method I

Consider the BIBD with parameter $t=2k+1$, $b=2(2k+1)$, $r=t-1$, $p=k\geq 2$, $\lambda=k-1$, that associated with either primitive root $x=2$ or $x=3$.

Setting x^0 to be treatment 1 and $x^1 \equiv x$ which is primitive root for both initial blocks in equations (3.7) and (3.8) below respectively, $m=2$,

Therefore the two initial blocks sequences are :

$$I_1= (x^0, x^m, x^{2m}, \dots x^{2k-2}) , m=2, , p = k \geq 2 \quad (3.7)$$

$$I_2 = (x^1, x^{m+1}, x^{2m+1}, \dots, x^{2k-1}), m=2, p = k \geq 2 \quad (3.8)$$

3.2.2.1 Construction of BISCOD when the number treatments is 5

The design construction method II performed function which design construction method I has done by generated every non-zero elements for primitive $x=2$

For $t=5$, $m=2$, $k=2$, $x=2$, then a BIBD with the two initial blocks exists

$I_1= (x^0, x^m, x^{2m}, \dots x^{2k-2})$ $I_2 = (x^1, x^{m+1}, x^{2m+1}, \dots, x^{2k-1})$, for $m=2$, $k= 2$, $x=2$

$I_1= (x^0,x^m)$

$=(2^0, 2^2) = (1,4)$

In Mod5=(1, 4)

$I_2 =(x^1, x^{m+1})$

$= (2^1, 2^{2+1})$

$= (2^1,2^3) = (2,8)$

In Mod5= (2, 3)

Therefore the two initial blocks sequences are: (1, 4) and (2, 3) in mod 5

Select first initial block sequence (1, 4)

Multiply the first initial block with every non-zero element of GF(5)=(0,1,2,3,4) to obtain initial sequences with 4 terms

1x1=1 1x2=2 1x3=3 1x4=4

4x1=4 4x2=8 4x3 12 4x4=16

In Mod5 for 4 initial sequences are :(1 2 3 4)

(4 3 2 1)

A universally optimal BISCOD is obtain cyclically for residual effects of first order with parameters t = 5, n = 20, k = 2.

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

From the above design each other treatment is being preceded by each treatment once

Select second initial block sequence (2, 3)

Multiply the second initial block with every non-zero element of GF(5)=(0,1,2,3,4) to obtain initial sequences with 4 terms

2x1=2 2x2=4 2x3=6 2x4=8

3x1=3 3x2=6 3x3=9 3x4=12

In mod5 for 4 initial sequences are : (2 4 1 3)

(3 1 4 2)

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 5, n = 20, k = 2

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

From the above design each other treatment is being preceded by each treatment once

3.2.2.2 Construction of BISCOD when the number of treatments is 7

The design construction method II also generated every non-zero elements of prime numbers of treatment that satisfy primitive x=3

For t=7, m=2, k=3, x=3 , then a BIBD with the two initial blocks exists

$I_1 = (x^0, x^m, x^{2m}, \ldots x^{2k-2})$ $I_2 = (x^1, x^{m+1}, x^{2m+1}, \ldots, x^{2k-1})$, for m=2, k= 3, x=3

$I_1 = (x^0, x^m, x^{2m})$

$= (3^0, 3^2\ 3^4) = (1, 9, 81)$

In Mod7= (1, 2, 4)

$I_2 = (x^1, x^{m+1}, x^{2m+1})$

$= (3^1, 3^{2+1}\ 3^{4+1})$

$= (3^1, 3^3\ 3^5) = (3, 27, 243)$

In Mod7= (3, 6, 5)

The two initial blocks sequences are (1, 2, 4) and (3,6,5) in mod 7

Select first initial block sequence (1,2, 4)

Multiply the first initial block with every non-zero elements of GF(7)=(0,1,2,3,4,5,6) to obtain initial sequences with 6 terms

1x1 1x2 1x3 1x4 1x5 1x6

2x1 2x2 2x3 2x4 2x5 2x6

4x1 4x2 4x3 4x4 4x5 4x6

We have 1 2 3 4 5 6

2 4 6 8 10 12

4 8 12 16 20 24

In Mod7 initial sequences are: 1 2 3 4 5 6

2 4 6 1 3 5

4 1 5 2 6 3

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 7, n = 42, k = 3

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

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

From the above design each other treatment is being preceded by each treatment twice

Select second initial block (3,6,5)

Multiply the second initial block with every non-zero elements of GF(7)=(0,1,2,3,4,5,6) to obtain initial sequences with 6 terms

3x1 3x2 3x3 3x4 3x5 3x6

6x1 6x2 6x3 6x4 6x5 6x6

5x1 5x2 5x3 5x4 5x5 5x6

We have 3 6 9 12 15 18

6 12 18 24 30 36

5 10 15 20 25 30

In Mod 7 initial sequences are : 3 6 2 5 1 4

6 5 4 3 2 1

5 3 1 6 4 2

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 7, N = 42, k = 3.

3 4 5 6 0 1 2 6 0 1 2 3 4 52 3 4 5 6 0 1 5 6 0 1 2 3 4

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

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

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

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

From the above design each other treatment is being preceded by each treatment twice

3.2.2.3 Construction of BISCOD when the number of treatments is 11

The design construction method II generated prime number of treatment which design construction method I cannot generated, such as number of treatments is 11

For t=11, m=2, k=5, x=2, then a BIBD with the two initial blocks exists

$I_1 = (x^0, x^m, x^{2m}, \dots x^{2k-2})$ $I_2 = (x^1, x^{m+1}, x^{2m+1}, \dots, x^{2k-1})$, for m=2, k= 2, x=2

$I_1 = (x^0, x^m, x^{2m}, x^{3m}, x^{4m})$

$=(2^0, 2^2, 2^4, 2^6, 2^8) = (1, 4, 16, 64, 256)$

In Mod11 = (1, 4, 5, 9, 3)

$I_2 = (x^1, x^{m+1}, x^{2m+1}, x^{3m+1}, x^{4m+1})$

$= (2^1, 2^{2+1}, 2^{4+1}, 2^{6+1}, 2^{8+1})$

$= (2^1, 2^3\ 2^5\ 2^7\ 2^9) = (2,8, 32, 128, 512)$

In Mod11=(2, 8, 10, 7, 6)

The two initial blocks sequences are : (1, 4, 5, 9, 3) and (2, 8, 10, 7, 6) in mod 11

Select first initial block sequence (1, 4, 5, 9, 3)

Multiply the first initial block with every non-zero element of GF (11) to obtain initial sequences with 10 terms

1x1	1x2	1x3	1x4	1x5	1x6	1x7	1x8	1x9	1x10
4x1	4x2	4x3	4x4	4x5	4x6	4x7	4x8	4x9	4x10
5x1	5x2	5x3	5x4	5x5	5x6	5x7	5x8	5x9	5x10
9x1	9x2	9x3	9x4	9x5	9x6	9x7	9x8	9x9	9x10
3x1	3x2	3x3	3x4	3x5	3x6	3x7	3x8	3x9	3x10

We have=

1	2	3	4	5	6	7	8	9	10
4	8	12	16	20	24	28	32	36	40
5	10	15	20	25	30	35	40	45	50
9	18	27	36	45	54	63	72	81	90
3	6	9	12	15	18	21	24	27	30

In mod11 initial sequences are:

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

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 11, n = 110, k = 5.

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

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

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

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

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

From the above design each other treatment is being preceded by each treatment 4 times

Select second initial block sequence (2, 8, 10, 7, 6)

Multiply the second initial block with every non-zero element of GF (11) to obtain initial sequences with 10 terms

2x1	2x2	2x3	2x4	2x5	2x6	2x7	2x8	2x9	2x10
8x1	8x2	8x3	8x4	8x5	8x6	8x7	8x8	8x9	8x10
10x1	10x2	10x3	10x4	10x5	10x6	10x7	10x8	10x9	10x10
7x1	7x2	7x3	7x4	7x5	7x6	7x7	7x8	7x9	7x10
6x1	6x2	6x3	6x4	6x5	6x6	6x7	6x8	6x9	6x10

We have

2	4	6	8	10	12	14	16	18	20
8	16	24	32	40	48	56	64	72	80
10	20	30	40	50	60	70	80	90	100
7	14	21	28	35	42	49	56	63	70
6	12	18	24	30	36	42	48	54	60

In mod11 initial sequences are :

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

A universally optimal BISCOD is obtained cyclically for residual effects of first order with parameters t = 11, n = 110, k = 5 is obtained.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

From the above design each other treatment is being preceded by each treatment 4 times

Table 3.2.1: Prime Numbers of Treatments (t) that satisfy Primitive root x =2 for Number of Periods, $p \geq 2$

Existing method		Modified method	
t=4m+1 at $m \geq 1$	Design Constructed	t = 2k + 1 $k \geq 2$	Design Constructed
5	Possible	5	Possible
11	Not Possible	11	Possible
13	Possible	13	Possible
19	Not Possible	19	Possible
37	Possible	37	Possible
61	Possible	61	Possible

Table 3.2.1, shows that existing method was unable to generate designs for some prime numbers of treatments that satisfy primitive root x=2, for $m \geq 1$ (1, 2, 3, …,). However, modified method is able to address the shortcoming indicated in the foregoing statement, in the sense that it can generate designs for any prime numbers of treatments for $k \geq 2$ (2,3,…,)

3.2.2.4 METHOD OF COMPARING DESIGNS

The method for special case of crossover design when number of period, p, is less than number of treatment, t, is referred to as Incomplete Sequence Crossover Design (ISCOD). The special case of crossover design in the foregoing statement was used for comparisons of designs by Kiefer (1975) and Hedayat et al (2006). Two subclasses in the entire class $\Omega_{t, n, p}$ for t denotes treatment, n denotes subject and p denotes period for ISCOD is universally optimal and follow the A, D, and E optimality.

The two subclasses are

(i) $\Omega^1 = \Omega^1_{t, n, p}$ which consisting of all designs in which each treatment is replicated n/t times in the last period.

(ii) $\Omega^2 = \Omega^2_{t, n, p}$, subclass of $\Omega_{t, n, p}$ consisting of all designs in which each treatment is replicated n/t times in the last period, no treatment is immediately preceded by itself in any of the treatment sequences of the design.

3.2.2.5 COMPARISONS AMONG DESIGNS CONSTRUCTED

- Designs from both Modified design construction method and Mithilesh and Archana existing design construction method were balanced and universally optimal. With respect to method in 3.2.2.4, each treatment was replicated n/t times in the last period in each design.
- Modified design construction method was efficient than Mithilesh and Archana existing design construction method in terms of generating prime number of treatments for design construction. From Table 3.2.1, Modified design construction method generated prime numbers, that Mithilesh and Archana existing design construction was inability to generate,

such as t= 11, 19

- Modified design construction method generated every non-zero elements of prime numbers of treatments that satisfy primitive root x=2 when m = 2. Mithilesh and Archana existing design construction method cannot generate every non-zero elements when m=2
- Modified design construction method cannot generate every non-zero elements of prime numbers of treatments that satisfy primitive roots x=2 when m < 2. Mithilesh and Archana existing design construction generated non-zero elements of prime numbers of treatments that satisfy primitive root x=2 when m= ≥ 0.5 (0.5, 1, 1.5, . . . ,)
- New class design construction method generated non-zero elements of prime numbers of treatments that satisfy primitive roots x=2 and 3

3.2.3 Model

$Y_{ijkq} = \mu + \tau_i + \beta_j + \gamma_k + £_{ijk}$

$$i = 1\ldots, .n,\ k = 1,\ldots,p;\ j = 1\ldots t$$

$Y_{ijkq}$is the milk concentration from the i^{th} experimental unit in the k^{th} period when treatment j allocated to it and q^{th} treatment preceded it in $(k-1)^{th}$ period (k.1)

μ is the overall mean

$\gamma_k$is the k^{th} period effect

τ_I is the i^{th} experimental unit (calf) effect

β_j is the j^{th} treatment (methionine) direct effect

$£_{ijk}$ is the random error

3.2.3.1 Estimation of Model Parameter

total corrected sum of squares

$$\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - \bar{y}_{\ldots})^2 = [\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (\bar{y}_{i..} - \bar{y}_{\ldots}) + (\bar{y}_{.j.} - \bar{y}_{\ldots}) + (y_{..k} - y_{\ldots}) + (\bar{y}_{ijk} - \bar{y}_{i..} - \bar{y}_{.j.} + \bar{y}_{..k} + y_{\ldots})]^2$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - \bar{y}_{\ldots})^2 = tp \sum_{i=1}^{u} (\bar{y}_{i..} - \bar{y}_{\ldots})^2 + np \sum_{j}^{t} (\bar{y}_{.j.} - \bar{y}_{\ldots})^2 + nt \sum_{k}^{p} (\bar{y}_{..k} - \bar{y}_{\ldots})^2 +$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - y_{i..} - y_{.j.} + y_{\ldots})^2 + 2\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{i..}\ \ y_{\ldots})(y_{.j.} - y\ )(y_{..k} - y_{\ldots}) +$$

$$2\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (\bar{y}_{i..} - \bar{y}_{\ldots})(y_{ijk} - \bar{y}_{i..} - \bar{y}_{.j.} + y_{\ldots}) + 2(\bar{y}_{..k} - \bar{y}_{\ldots})(y_{ijk} - \bar{y}_{i..} - \bar{y}_{.j.} + \bar{y}_{\ldots}) + 2(\bar{y}_{.j.} - \bar{y}_{\ldots})$$

$$(y_{ijk} - \bar{y}_{i..} - \bar{y}_{.j.} - \bar{y}_{\ldots})\ 2(\bar{y}_{..k} - \bar{y}_{\ldots})(\bar{y}_{ijk} - \bar{y}_{i..} - \bar{y}_{.j.} + \bar{y}_{\ldots})$$

To estimate μ, τ_i, β_j, γ_k by least squares sum of squares of the errors

$$Q = \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} Q_{ijk} = \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (\bar{y}_{ijk} - \mu - \tau_i - \beta_j - \gamma_k)^2$$

$$dQ / d\mu = -2 \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - \mu - \tau_i - \beta_j - \gamma_k) = 0$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk} - ntp\mu - tp\sum_{i=1}^{u} \tau i - np\sum_{j=1}^{t} \beta j - nt\sum_{k=1}^{p} \gamma_{k=0}$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk} - ntp\mu = 0$$

$$ntp\mu = \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk}$$

$$\mu = [(\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk})] / ntp$$

$$dQ / d\tau = -2 \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - \mu - \tau_i - \beta_j - \gamma_k) = 0$$

$$\sum_{j}^{t}\sum_{k}^{p} y_{ijk} - tp\mu - tp\tau_i - p\sum_{j=1}^{t}\beta j - t\sum_{k=1}^{p} \gamma_{k=0}$$

$$\sum_{j}^{t}\sum_{k}^{p} y_{ijk} - tp\mu - tp\tau_i$$

$$\tau_i = [(\sum_{j=1}^{t}\sum_{k=1}^{p} y_{jk}) / tp] - \mu$$

$$dQ / d\beta = -2 \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (yijk - \mu - \tau_i - \beta_j - \gamma_k) = 0$$

$$\sum_{i=1}^{n}\sum_{k=1}^{p} y_{ijk} - np\mu - p\sum_{i=1}^{u}\tau i - np\beta_j - n\sum_{k=1}^{p} \gamma_{k=} 0$$

$$\sum_{i=1}^{n}\sum_{k=1}^{p} y_{ijk} - np\mu - np\beta_j = 0$$

$$\beta_j = [(\sum_{i=1}^{n}\sum_{k=1}^{p} y_{ik}) / np] - \mu$$

$$dQ / d\gamma = -2 \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (yijk - \mu - \tau_i - \beta_j - \gamma_k) = 0$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t} y_{ijk} - nt\mu - t\sum_{i=1}^{u}\tau i - n\sum_{j=1}^{t}\beta j - nt\,\gamma_{k=} 0$$

$$\sum_{i=1}^{n}\sum_{j=1}^{t} y_{ijk} - nt\mu - nt\,\gamma_{k=} 0$$

$$\gamma_k = = [(\sum_{i=1}^{n}\sum_{j=1}^{t} y_{ij}) / nt] - \mu$$

Sum of Squares (SS)

$$SS_{subject\ (unit)} = [(\sum_{j=1}^{t}\sum_{k=1}^{p} y_{jk})^2 / tp] - (\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk})^2 / ntp$$

$$SS_{t\,reatment} = [(\sum_{i=1}^{n}\sum_{k=1}^{p} y_{ik}) / np] - (\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk})^2 / ntp$$

$$SS_{period} = = [(\sum_{i=1}^{n}\sum_{j=1}^{t} y_{ij})^2 / nt] - (\sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} y_{ijk})^2 / ntp$$

$$SS_{Total} = \sum_{i=1}^{n}\sum_{j=1}^{t}\sum_{k=1}^{p} (y_{ijk} - \bar{y}\ldots)^2$$

$$SS_{Residual(Error)} = SS_{Total} - SS_{subject\ (unit)} - SS_{t\,reatment} - SS_{period}$$

Mean Square(MS)

$MS_{subject\ (unit)} = (SS_{subject\ (unit)}) / n-1$

$MS_{t\,reatment} = (SS_{t\,reatment}) / t-1$

$MS_{period} = (SS_{period}) / p-1$

$MS_{Residual(Error)} = (SS_{Residual(Error)}) / [(n-1) (t-1) (p-1)]$

Test Statistic

$F_{o\,(}$subject) $= (MS_{subject\ (unit)}) / MS_{Residual(Error)}$

$F_{o\,(}$treatment) $= (MS_{treatment}) / MS_{Residual(Error)}$

$F_{o\,(}$period) $= (MS_{period}) / MS_{Residual(Error)}$

3. 2.3.2 Hypothesis To be Tested

Hypothesis testing is carried out to know if there is significant difference in treatment effects; and residual effect

H_0 : there is no significant difference in treatment effects

H_1: Not H_0

H_0 : there is no significant difference in residual effect effects

H_1: Not H_0

Decision rule: reject H_0 if p-value is less than $\alpha - value$

CHAPTER FOUR

ANALYSIS OF A CROSSOVER EXPERIMENT

4.0 Introduction

This chapter presents data to illustrate practical application of the existing and modified methods that were considered in this thesis. Appropriate analysis and discussion of results arising there are presented in sections 4.1,4.2 and 4.4. Meanwhile, results were presented for the existing design construction method algorithm**,** modified design construction method first algorithm and modified design construction method second algorithm.

4.1 Data Description

The data was obtain from design and analysis of experiments book by Gill (1978) and was on two period crossover experiment used to study Methionine (amino acid) requirement for milk protein concentration production in dairy calves. Five doses of Methionine A= 70%, B= 85%, C= 100%, D=115%, E= 130% were used for twenty calves for an incomplete sequence with five treatments; twenty sequences; and two period. The main purpose of the experiment was to investigate whether the direct treatment effects and the associated residual or carry over effects are significant

4.2 Data for the Analysis

Table 4.2.1: Data on Existing Design Construction Method Sequence

Sequence

Period	1	2	3	4	5	6	7	8	9	10
1	0.49A	0.42B	0.45A	0.73C	0.20A	0.66D	0.54A	0.81E	0.71B	0.76C
2	0.80B	0.45A	0.92C	0.48A	0.67D	0.40A	0.96E	0.69A	0.80C	0.69B

Sequence

Period	11	12	13	14	15	16	17	18	19	20
1	0.80B	0.65D	0.48B	0.70E	0.86C	1.18D	0.87C	0.63E	1.20D	1.19E
2	0.97D	0.50B	0.74E	0.77B	1.02D	1.22C	0.93E	0.67C	1.26E	1.38D

Table 4.2.2: Data for Modified Design Construction Method First Sequence

Sequence

Period	1	2	3	4	5	6	7	8	9	10
1	0.20A	0.48B	0.73C	0.65D	0.63E	0.71B	0.86C	1.20D	0.81E	0.49A
2	0.67D	0.74E	0.48A	0.50B	0.67C	0.80C	1.02D	1.26E	0.69A	0.80B
Period	11	12	13	14	15	16	17	18	19	20
1	0.76C	1.18D	1.19E	0.54A	0.42B	0.66D	0.70E	0.45A	0.80B	0.87C
2	0.69B	1.22C	1.38D	0.96E	0.45A	0.40A	0.77B	0.92C	0.97D	0.93E

Table 4.2.3: Data for Modified Design Construction Method Second Sequence

Sequence

Period	1	2	3	4	5	6	7	8	9	10
1	0.71B	0.86C	1.20D	0.81E	0.49A	0.66D	0.70E	0.45A	0.80B	0.87C
2	0.80C	1.02D	1.26E	0.69A	0.80B	0.40A	0.77B	0.92C	0.97D	0.93E

Sequence

Period	11	12	13	14	15	16	17	18	19	20
1	0.20 A	0.48B	0.73C	0.65D	0.63E	0.76C	1.18D	1.19E	0.54A	0.42B
2	0.67D	0.74E	0.48A	0.50B	0.67C	0.69B	1.22C	1.38D	0.96E	0.45A

4.3 Result of the Analysis

Table 4.3.1: Analysis of Variance for Existing Design Construction Method Sequences

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F- Ratio	P- Value
Sequence	1	0.01	0.01	0.11	0.6553
Treatment	4	1.38	0.35	3.89	0.0001
Period	1	0.05	0.05	0.56	0.2706
Residual(Error)	33	2.97	0.09	1.48	0.2230
Total	39	4.41			

Table4.3.2: Analysis of Variance for Modified Design Construction Method I for First Sequence

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F- Ratio	P- Value
Sequence	1	0.01	0.01	0.09	0.7826
Treatment	4	1.09	0.27	2.45	0.0012
Period	1	0.06	0.06	0.55	0.2378
Residual(Error)	33	3.63	0.11	1.57	0.1846
Total	39	4.79			

Table4.3.3: Analysis of Variance for Modified Design Construction Method I for Second Sequence

Source of Variation	Degree of Freedom	Sum of Square	Mean Square	F- Ratio	P- Value
Sequence	1	0.02	0.02	0.29	0.6182
Treatment	4	0.41	0.10	1.43	0.0001
Period	1	0.11	0.11	1.57	0.0001
Residual(Error)	33	2.31	0.07	1.67	0.0001
Total	39	2.85			

4.4 Sequences of Non-Zero Elements of Prime Number of Treatments

Table4.4.1: Existing Design Construction Method Sequences for Primitive Root x=2

V	x	k	m ≥ 0.5	First Sequences	Second Sequences
5	2	2	0.5, 1	1, 4	2, 3
13	2	6	0.5, 1, 1.5, 2, 2.5, 3	1, 4, 3, 12, 9, 10	2, 8, 6, 11, 5, 7
37	2	18	0.5, 1,1.5, 2, 2.5, 3, 3.5, 4,4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9	1,4,16,27,34,25,26,30,9,36,33,21, 10,3,12,11,7,28	2,8,32,17,31,13,15,23,18,35,29,5, 20,6,24,22,14,19
61	2	30	0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5, 9, 9.5, 10, 10.5, 11, 11.5, 12, 12.5, 13, 13.5, 14, 14.5, 15	1,4,16,3,12,48,9,36,22,27,47,5,20, 19,15,60,57,45,58,49,13,52,25,39, 34,14,56,41,42,46	2,8,32,6,24,35,18,11,44,54,33,10, 40,38,30,59,53,29,55,37,26,43,50, 17,7,28,51,21,23,31

Table4.4.2: Modified Design Construction Method I Sequences for Primitive Root x=2

V	x	k	m= 2	First Sequences	Second Sequences
5	2	2	2	1, 4	2, 3
11	2	5	2	1,4,5,9,3	2,8,10,7,6
13	2	6	2	1, 4, 3, 12, 9, 10	2, 8, 6, 11, 5, 7
19	2	9	2	1,4,16,7,9,17,11,6,5,	2,8,13,14,18,15,3,12,10
37	2	18	2	1,4,16,27,34,25,26,30,9,36,33,21, 10,3,12,11,7,28	2,8,32,17,31,13,15,23,18,35,29,5, 20,6,24,22,14,19
61	2	30	2	1,4,16,3,12,48,9,36,22,27,47,5,20, 19,15,60,57,45,58,49,13,52,25,39, 34,14,56,41,42,46	2,8,32,6,24,35,18,11,44,54,33,10, 40,38,30,59,53,29,55,37,26,43,50, 17,7,28,51,21,23,31

Table4.4.3: New Class Design Method Sequence for Primitive Roots x=2 and 3

V	x	k	m=2	First Sequences	Second Sequences
5	2	2	2	1, 4	2, 3
7	3	3	2	1,2,4	3,6,5
11	2	5	2	1,4,5,9,3	2,8,10,7,6
13	2	6	2	1, 4, 3, 12, 9, 10	2, 8, 6, 11, 5, 7
17	3	8	2	1, 9, 13, 15, 16, 8, 4, 2	3,10, 5, 11, 14, 7, 12, 6
19	2	9	2		
37	2	18	2	1,4,16,7,9,17,11,6,5,	2,8,13,14,18,15,3,12,10
				1,4,16,27,34,25,26,30,9,36,33,21,	2,8,32,17,31,13,15,23,18,35,29,5,
61	2	30	2	10,3,12,11,7,28	20,6,24,22,14,19
				1,4,16,3,12,48,9,36,22,27,47,5,20,	2,8,32,6,24,35,18,11,44,54,33,10,
				19,15,60,57,45,58,49,13,52,25,39,	40,38,30,59,53,29,55,37,26,43,50,
				34,14,56,41,42,46	17,7,28,51,21,23,31

4.5 Discussion of the Results

The result of analysis is summarized as presented in Tables 4.3.1 to 4.3.3 as follow:

i Essentially we have considered sequences for existing design construction method and modified design construction method I

ii From the Table 4.3.1, it was observed that treatment effect p-value(0.0001) < α value at both 1% and 5%, therefore H_0 is rejected which mean effect is significant.

iii From the Table 4.3.1, it was observed that residual effect p-value(0.2230) > α value at both 1% and 5%, therefore we do not have sufficient reason to reject H_0 which means no significant difference

iv From the Table 4.3.2, it was observed that treatment effect p-value (0.0012) < α value at both 1% and 5%, therefore we reject H_0 which means the effect is significant.

v From the Table 4.3.2, it was observed that residual effect p-value (0.1846) > α value at both

1% and 5%, therefore we do not have sufficient reason to reject H_0 which mean no significant difference

vi From the Table 4.3.3, it was observed that treatment effect p-value(0..0001) < α value at both 1% and 5%, therefore we reject H_0 which mean effect is significant.

vii From the Table 4.3.3, it was observed that residual effect p-value (0.0001) < α value at both 1% and 5%, therefore we reject H_0 which mean effect is significant.

viii From the Table 4.4.1, it was observed that values of $m \geq 0.5$ for the two initial blocks sequences for the Existing design construction method for primitive root x=2.

ix From the Table 4.4.2, it was observed that value of m=2, for the two initial blocks sequences for the modified design construction method I for primitive root x=2.

x From the Table 4.4.3, it was observed that value of m=2, for the two initial blocks sequences for the modified design construction method II for primitive roots x=2 and 3

xi From Table 4.3.1 to 4.3.3, it was observed that treatment effect MSE is 0.35 for existing design construction method sequence, 0.27 for modified design construction method I first sequence and 0.10 for modified design method I second sequence respectively; while residua effect MSE is 0.09 for existing design method sequence,0.11 for modified design construction method I first sequence and 0.07 for modified design construction method I second sequence.

CHAPTER FIVE

SUMMARY, CONCLUSION AND RECOMMENDATION

5.0 Introduction

This chapter is on summary, conclusion and recommendation of the work carried out in this study.

5.1 Discussion of Findings

The findings of this study were that:

i prime numbers of treatments that satisfied primitive roots x=2 and 3 include 5, 7, 11, 13, 17,19, 37, 61 were shown in this study

ii design using a modified design construction method I, was generated for all prime numbers for primitive root x = 2;

iii construction method for a new class design that generates all prime numbers that satisfied primitive roots x=2 and 3 was developed;

iv residual effects of modified construction method was significant

v measurement of residual effects for first order of each treatment increase as the sequence number increases;

vi each other treatment is being preceded by each treatment (k-1) times;

vii modified design construction method was validated that each treatment was replicated n/t times in the last period in each design

viii from Table 4.3.1 both treatment and residual effects are significant and non-significant respectively at both 5% and 1% significant level for existing design construction method sequence;

ix from Table 4.3.2 both treatment and residual effects are significant and non-significant respectively at both 5% and 1% significant level for modified design construction method first sequence;

x from Table 4.3.3 both treatment and residual effects are significant at both 5% and 1% significant level for modified design construction method second sequence;

xi MSE for treatment effect is 0.35 for existing design construction method sequence, 0.27 for modified design method first algorithm and 0.10 for modified design method second algorithm from Table 4.3. 1 to 4.3.3 respectively; also, MSE for residual effect is 0.09 for existing design method algorithm, 0.11 for modified design method first algorithm and 0.07 for modified design construction method second sequence from Table 4.3.1 to 4.3.3 respectively; and

xii computer algorithm that was developed to construct design performed the same function with manual algorithm.

5.2 Summary

This summary of this study were that:

i construction method which is modified method generates all prime numbers of treatments that satisfied primitive root $x=2$ with $m=2$ and $k\geq 2$ including those prime numbers which existing design construction method cannot generated with $m\geq 1$ for prime numbers of treatments t and $m\geq 0.5$

ii construction method for a new class design generates all prime numbers of treatment that satisfied primitive roots $x=2$ and 3;

iii treatment effect is significant at both 1% and 5% significance level for existing method sequence, modified method first sequence and modified method second sequence;

iv residual effect is not significant at both 5% and 1%significance level for both existing method algorithm and modified method first sequence, while significant at both 1% and 5% significance level for modified method second sequence; and

v MSE of modified method second sequence is the least among MSE of existing method sequence, modified method first algorithm and modified method second sequence for both treatment effect and residual effect.

5.3 Conclusion

Modified design construction method and Existing design construction method were both universally optimal balanced design for replicated each treatment n/t times in the last period Modified design construction method was more efficient than existing design construction method for generating prime numbers of treatments that existing design construction method was inability to generate.

5.4 Recommendation

- to generate any prime numbers of treatment that satisfy primitive root x=2 for any prime numbers of treatments modified design construction method is recommended
- to generate any prime numbers of treatment that satisfy primitive roots x=2 and 3 for prime numbers of treatments modified design construction method is recommended

5.5 Contributions to Knowledge and Suggestions for Future Research

5.5.1 Contribution to Knowledge

This study has contributed to knowledge through the following:

i Shows prime numbers of treatment that satisfy primitive root x=2

ii Construction of modified method of BISCOD for residual effects of first order for all prime numbers that satisfy primitive root x=2

iii Construction of new class method of BISCOD for residual effects of first order for all prime numbers of treatment that satisfy primitive roots x=2 and 3

5.5.2 Suggestion for Future Research

i Construction of BISCOD for residual effects of first order for all prime numbers satisfy other primitive root apart from x=2 and 3

ii Construction of balanced complete sequence for residual effects of first order for all prime numbers of treatment that satisfy primitive root x=2and 3

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APPENDIX

```
# #FOR 1st INITIAL BLOCK (1st phase)
# note:  mod(81,7) = 81-7*floor(81/7)
# using x = 2 and v = 5,11,13

initialBLK.1a=function(x){
m=2
v = c(5,11,13)
k=(v-1)/2
x1 = x^0
x2=x^m
x3=x^(2*m)
x4=x^(3*m)
x5=x^(4*m)
x6=x^(5*m)
#when v = 5
resultv5 = c(x1,x2)
firstinitialv5= c(x1-v[1]*floor(x1/v[1]), x2-v[1]*floor(x2/v[1]))
#when v = 11
resultv11 = c(x1,x2,x3,x4,x5)
firstinitialv11=    c(x1-v[2]*floor(x1/v[2]),    x2-v[2]*floor(x2/v[2]),x3-v[2]*floor(x3/v[2]),x4-
v[2]*floor(x4/v[2]),x5-v[2]*floor(x5/v[2]))
#when v = 13
resultv13 = c(x1,x2,x3,x4,x5,x6)
firstinitialv13=    c(x1-v[3]*floor(x1/v[3]),    x2-v[3]*floor(x2/v[3]),x3-v[3]*floor(x3/v[3]),x4-
v[3]*floor(x4/v[3]),x5-v[3]*floor(x5/v[3]),x6-v[3]*floor(x6/v[3]))
result5=c(resultv5,firstinitialv5)
result11=c(resultv11,firstinitialv11)
result13=c(resultv13,firstinitialv13)
five=matrix(result5,nrow=2,byrow=TRUE)
colnames(five) = c("x1","x2")
```

```
rownames(five) = c("real","mod5")
print(five)
eleven = matrix(result11,nrow=2,byrow=TRUE)
colnames(eleven) = c("x1","x2","x3","x4","x5")
rownames(eleven) = c("real","mod11")
print(eleven)
thirteen = matrix(result13,nrow=2,byrow=TRUE)
colnames(thirteen) = c("x1","x2","x3","x4","x5","x6")
rownames(thirteen) = c("real","mod13")
print(thirteen)
}

#example 1: when x = 2
initialBLK.1a(2)

        x1  x2
   real 1   4
   mod5 1   4
       x1  x2  x3  x4   x5
  real  1   4  16  64  256
mod11   1   4   5   9    3
       x1 x2  x3  x4   x5    x6
  real  1  4  16  64  256  1024
mod13   1  4   3  12   9     10
################################################################################
```

```
##############################################################################################
#FOR INITIAL BLOCK (2nd phase)

# using x = 2 and v = 5,11,13

initialBLK.2a=function(x){
m=2
v = c(5,11,13)
k=(v-1)/2
x1 = x^1
x2=x^(m+1)
x3=x^(2*(m+1))
x4=x^(3*(m+1))
x5=x^(4*(m+1))
x6=x^(5*(m+1))
#when v = 5
resultv5 = c(x1,x2)
firstinitialv5= c(x1-v[1]*floor(x1/v[1]), x2-v[1]*floor(x2/v[1]))
#when v = 11
resultv11 = c(x1,x2,x3,x4,x5)
firstinitialv11= c(x1-v[2]*floor(x1/v[2]), x2-v[2]*floor(x2/v[2]),x3-v[2]*floor(x3/v[2]),x4-v[2]*floor(x4/v[2]),x5-v[2]*floor(x5/v[2]))
#when v = 13
resultv13 = c(x1,x2,x3,x4,x5,x6)
firstinitialv13= c(x1-v[3]*floor(x1/v[3]), x2-v[3]*floor(x2/v[3]),x3-v[3]*floor(x3/v[3]),x4-v[3]*floor(x4/v[3]),x5-v[3]*floor(x5/v[3]),x6-v[3]*floor(x6/v[3]))
result5=c(resultv5,firstinitialv5)
result11=c(resultv11,firstinitialv11)
result13=c(resultv13,firstinitialv13)
```

```
five=matrix(result5,nrow=2,byrow=TRUE)
colnames(five) = c("x1","x2")
rownames(five) = c("real","mod5")
print(five)
eleven = matrix(result11,nrow=2,byrow=TRUE)
colnames(eleven) = c("x1","x2","x3","x4","x5")
rownames(eleven) = c("real","mod11")
print(eleven)
thirteen = matrix(result13,nrow=2,byrow=TRUE)
colnames(thirteen) = c("x1","x2","x3","x4","x5","x6")
rownames(thirteen) = c("real","mod13")
print(thirteen)
}
#example 3: when x = 2
initialBLK.2a(2)

      x1  x2
 real  2   8
mod5  2  3
       x1  x2  x3  x4    x5
real   2   8   64  512  4096
mod11  2   8    9   6     4
       x1  x2  x3   x4    x5    x6
real    2   8   64  512  4096  32768
mod13  2    8   12   5     1      8
##################################################################

#CYCLIC DEVELOPMENT
#from x = 2 and v = 5
a = 1:5
v = c(5,11,13)
```

```
x1 = c(a[1]*a[1],a[1]*a[2],a[1]*a[3],a[1]*a[4])
x2 = c(a[4]*a[1],a[4]*a[2],a[4]*a[3],a[4]*a[4])
t = c(a[1]*a[1],a[1]*a[2],a[1]*a[3],a[1]*a[4],a[1]*a[5])
p = c(a[4]*a[1],a[4]*a[2],a[4]*a[3],a[4]*a[4],a[4]*a[5])
print(p)
s = c((p[1]-v[1]*floor(p[1]/v[1])),(p[2]-v[1]*floor(p[2]/v[1])),(p[3]-v[1]*floor(p[3]/v[1])),(p[4]-
v[1]*floor(p[4]/v[1])))
d1 = c((p[1]-v[1]*floor(p[1]/v[1])),(p[2]-v[1]*floor(p[2]/v[1])),(p[3]-v[1]*floor(p[3]/v[1])),(p[4]-
v[1]*floor(p[4]/v[1])),(p[5]-v[1]*floor(p[5]/v[1])))


#result from first transformation
first = data.frame(x1,s)
transform = t(first)

#CYCLIC DEVELOPMENT DETAILS

# s1 = c(1mod5,2mod5,3mod5,4mod5,5mod5)
# s2 = c(4mod5,5mod5,1mod5,2mod5,3mod5)

s1 = c((a[1]-v[1]*floor(a[1]/v[1])),(a[2]-v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])),(a[4]-
v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])))
s2 = c((a[4]-v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])),(a[1]-v[1]*floor(a[1]/v[1])),(a[2]-
v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])))
s12 = t(data.frame(s1,s2))

s1 = c((a[2]-v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])),(a[4]-v[1]*floor(a[4]/v[1])),(a[5]-
v[1]*floor(a[5]/v[1])),(a[1]-v[1]*floor(a[1]/v[1])))
s2 = c((a[3]-v[1]*floor(a[3]/v[1])),(a[4]-v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])),(a[1]-
v[1]*floor(a[1]/v[1])),(a[2]-v[1]*floor(a[2]/v[1])))
s34 = t(data.frame(s1,s2))
```

```
s1 = c((a[3]-v[1]*floor(a[3]/v[1])),(a[4]-v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])),(a[1]-
v[1]*floor(a[1]/v[1])),(a[2]-v[1]*floor(a[2]/v[1])))
s2 = c((a[2]-v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])),(a[4]-v[1]*floor(a[4]/v[1])),(a[5]-
v[1]*floor(a[5]/v[1])),(a[1]-v[1]*floor(a[1]/v[1])))
s45 = t(data.frame(s1,s2))

s1 = c((a[4]-v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])),(a[1]-v[1]*floor(a[1]/v[1])),(a[2]-
v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])))
s2 = c((a[1]-v[1]*floor(a[1]/v[1])),(a[2]-v[1]*floor(a[2]/v[1])),(a[3]-v[1]*floor(a[3]/v[1])),(a[4]-
v[1]*floor(a[4]/v[1])),(a[5]-v[1]*floor(a[5]/v[1])))
s56 = t(data.frame(s1,s2))

#combining cycles (in form of matrices)
s123456 = cbind(s12,s34,s45,s56)
colnames(s123456) = c(1:20)
rownames(s123456) = c("mod5","mod5")
print(s123456)

      1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
mod5 1  2 3 4 0 2 3 4 0 1  3  4  0  1  2  4  0  1  2  3
mod5 4  0 1 2 3 3 4 0 1 2  2  3  4  0  1  1  2  3  4  0
```