Glimpses of Basic Research in Design of Experiments at IASRI

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1. Introduction

The basic premise of the creation of a statistical section was to provide advisory on designing agricultural experiments to the state departments of agriculture and animal husbandry, to help them in analysis of data and interpretation of results. In the process of advisory, a need was felt to develop theories and designs and this laid the foundation of basic research in Design of Experiments with applications in solving complicated problems of agricultural research to bridge the gaps in the existing knowledge. Ever since then there has been a focused attention on basic research in design of experiments. The Institute has maintained pace with the developments at international level and for this reason the school of Design of Experiments at the Institute occupies a place of pride nationally and internationally. The research work carried out in Design of Experiments has been published in the International and National Journals of repute with high impact factors. As a consequence of important contributions made in Design of Experiments, several text books and monographs have been brought out which have a widespread citation.

The research work on theoretical developments in Design of Experiments was initiated during the decade of 1950. Many important contributions have been made in developing new methods of construction and analysis of experiments; in particular in finding suitable confounded designs for asymmetrical (or, mixed) factorials. The decade of 1960 saw many major contributions in designs for factorial experiments, rotatable and other response surface designs and designs for experiments with mixtures. The intense research activity in the area of design and analysis of experiments has continued rigorously throughout. The major emphasis has been obtaining optimal / efficient and robust designs for agricultural and allied sciences.

Some of the areas which received special attention included block designs (efficiency- and partially efficiency- balanced designs); weighing designs, crossover designs, orthogonal arrays and their application in obtaining fractional factorial plans, optimal block and row-column designs for making all the possible pair wise treatment comparisons, robust designs against the disturbances like loss of data, interchange and exchange of treatments, outliers, etc. Use of combinatorial designs in efficient survey sampling plans with unequal probabilities leading thereby to controlled selection was another major contribution. The use of mixed orthogonal arrays as Balanced Repeated Replications in the variance estimation of a non-linear statistic from a large scale complex survey data was an original contribution of the Institute.

More recently, the institute has undertaken basic research in optimality aspects of designs for test treatments versus control treatments comparisons. The comparisons are made with differential precision. The optimality aspects of block designs with nested blocks and nested rows and columns have been extensively studied. Similarly, the optimality aspects of designs with correlated observations, presence of trend in the observations within a block, designs for diallel and double cross experiments, designs for bioassays, designs for micro-array experiments, designs for crop sequence experiments, designs for estimation of competition effects from neighboring units, designs for two-way heterogeneity setting and a connection between these designs and block designs with two non-interacting sets of treatments, etc. are some of the major basic research contributions that have been accepted at an international level. We begin with the concepts of optimality and robustness in designed experiments. In Section 3 we give the developments in the theory of design of experiments concerning single factor experiments. Section 4 is devoted to multi-factor experiments and other important considerations are given in Section 5.

2. Optimality and Robustness of Designs

In the initial stages of development of experimental designs, emphasis was laid on constructing designs that were in some sense as symmetric as possible in their treatment of the statistical parameters of interest (for example, randomized complete block designs, balanced incomplete block designs, Latin square designs, Youden square designs, etc.). Such designs yielded "information matrices" (coefficient matrices of the reduced normal equations for estimation of treatment effects) that, especially in the pre-computer age, made statistical calculations easy; the designs had aesthetic appeal to mathematicians and often had algebraic or geometric representations that helped one to understand and construct them; and the symmetric treatment of parameters of interest seemed a reasonable property that made such designs yield statistical estimators that looked intuitively as accurate as possible for the given number of observations.

The advent of high speed computers; the realization of the importance and need to choose and adopt an experimental design that is best according to some well defined statistical criterion, led to the development of a subject like optimality of designs. The theory of optimal designs was almost non-existent till about the end of the Second World War, except for a remarkable early paper by Smith and the important paper of Wald. Professor Jack K. Kiefer initiated the serious and rigorous work on optimality aspects of designs. For the given experimental situation and an inference problem, there are a number of designs available, called a class of designs, which can be used to achieve some specified set of objectives. The choice of an appropriate design for a particular setting depends upon (a) the inference problem whose answer is sought for; (b) the class of designs in which choice is to be made (the class should have more than one design); and (c) the criterion or criteria to be used for the selection of the design. To be specific,

*A design d^* is said to be ψ-optimal for a given inference problem on η, a set of parametric function, in a class of competing designs **D** with some specified parameters, if d^* minimizes ψ [information matrix of best linear unbiased estimators (BLUE) of η] over **D**. The function ψ satisfies some pre-defined properties. It could be average variance of BLUE of η, generalized variance of BLUE of η, maximum variance of the elements of BLUE of η, etc.*

Some commonly used optimality criteria in the literature are A-optimality, D-optimality, E-optimality, MV-optimality, S-optimality, MS optimality, ϕ_p - optimality, universal optimality, DS-optimality, G-optimality, etc. The significant results obtained on the optimality aspects of designs are given in the concerned sections.

Optimal design theory has been developed and studied under what may be called as ideal conditions. Accidents and disturbances do occur even in a well-planned experiment and they render even an optimal design perform poorly and results in loss in efficiency. Various disturbances that commonly occur are – (i) missing observations(s), (ii) exchange of a treatment, (iii) interchange of a pair of treatments, (iv) presence of outlier(s), (v) presence of a systematic trend in the experimental units, (vi) model inadequacies, etc. In the presence of one or more of these disturbances even an optimal design may be poor. This realization is the motivation to the development of designs that are robust against one or more of the above disturbances. A design *d* is said to be robust against one or more disturbances if it remains insensitive to the presence of one or more disturbances in terms of design properties. To be specific, *consider a design d having some property "A" is subjected to some accident or disturbance. If the resulting design* d^* *obtained after the accident also possesses property "A", then the design is said to be robust against the accident.* The property *A* could be connectedness; variance balance; optimality; orthogonal factorial structure; efficiency, etc. The results obtained on the robustness aspects of designs are given in section 5.6.

3. Single Factor Experiments

In this section we describe the results on optimality aspects of designs for unstructured treatments also termed as varietal designs or single factor designs.

3.1 Block designs

We begin with the simplest experimental setting where there is only one blocking system. The inference problem being addressed is that of complete set of orthonormalized treatment contrasts or all possible pair wise treatment comparisons.

Incomplete block designs for all pair wise treatment comparisons

Balance in incomplete block (BIB) designs is a desirable statistical property. In literature, the term balance has been used in several senses viz., variance balance, efficiency balance, generalized efficiency balance and pair wise balance. While variance balance, efficiency balance and generalized efficiency balance are based on statistical properties, pair wise balance is a combinatorial property. A general method of construction of binary variance balanced block designs with unequal block sizes under a heteroscedastic model has been obtained. The method begins with a pair wise balanced design which is very easy to obtain and then converts it into a variance balanced design. It has been shown that the existence of a pair wise balanced design implies the existence of a binary variance-balanced design. All the designs hitherto known in the literature can be obtained from this general method of construction. An exhaustive catalogue of binary balanced block designs has been prepared for average replication smaller than 31 along with their resolvability status. These designs are universally optimal over a wide class of designs. The catalogue also includes the binary balanced block designs under the heteroscedastic model where intra block variances are assumed to be proportional to non-negative real power of block sizes. The resolvability status of these designs is also indicated. Several new methods of construction of *n*-ary variance balanced block designs have been given.

Partially Balanced Incomplete Block (PBIB) designs are an important class of incomplete block designs that can be used to economize on the use of experimental material. Some results on non-existence of PBIB designs with *m*-associate classes have been obtained by exploiting the complementary property of block designs. Some new group divisible and nested group divisible designs have been identified. Some new 3-class association schemes along with method of construction of PBIB designs based on these schemes have been obtained. A catalogue containing parameters of PBIB (3) designs has been prepared and made available on web.

The concept of partially efficiency balanced designs and simple partially efficiency balanced designs were introduced. In simple partially efficiency balanced designs, some contrasts are estimated with full efficiency.

Optimality aspects of block designs (universal optimality, E-optimality, etc.) have been studied under the usual fixed effects and mixed effects models.

Resolvable block designs

From practical considerations of the experimenters, the use of incomplete block designs becomes restrictive because all the treatments do not appear in adjacent piece of land and, therefore, the demonstration of variety effect / treatment effect in the field cannot be made. To overcome this problem, it is recommended that resolvable block designs with smaller block sizes may be used. A resolvable block design is a design in which the blocks can be grouped in such a way that every treatment appears once in each group; in other words, each group is a complete replication. Resolvable block designs have been studied by various authors in the literature. Resolvable solutions of BIB designs and PBIB designs are available. A simple class of resolvable block designs is the Lattice designs (square lattice, rectangular lattice, cubic lattice and circular lattice), but these solutions are available for a limited number of varieties and block sizes. For the benefit of the experimenters, a comprehensive catalogue of Lattice designs has been prepared. These designs have been compiled and brought out in the form of a technical bulletin for a ready reference of experimenters. The online generation of these designs is possible from IASRI web page. Catalogues of resolvable BIB designs and binary balanced block designs have also been prepared.

In agricultural experiments, the number of varieties is not fixed and the experimenter has to choose number of replications as per experimental resources. BIB designs, PBIB designs, cyclic designs, etc. may not meet the requirements of the experimenters as these designs would require many replications. Similarly the use of Lattice designs also becomes restrictive because of the restriction on number of treatments. α-designs are another class of resolvable incomplete block designs with number of treatments being a composite number. These designs can be generated in two and three replications also. The block size of these designs is a factor of number of treatments. For the benefit of the experimenters, a comprehensive catalogue of efficient α-designs for $6 \le v(=sk) \le 150$, $2 \le r \le 5$, $3 \le k \le 10$ and $2 \le s \le 15$ has been prepared along with lower bounds to A- and D- efficiencies and generating arrays. Here v is the number of treatments, r is the number of replications and k is the block size. Several designs obtained are more efficient than the corresponding designs available in the literature. A module for computer aided generation of α-designs has also been prepared. A randomized layout of these designs can be generated through Design Resources Server (http://www.iasri.res.in/design/Alpha/Home.htm).

Minimally connected designs with extra observations

For cost effective utilization of experimental resources, it is desired that the experiment be run in minimum possible number of experimental units. To ensure that all possible pair wise treatment comparisons are possible in a block design, the minimum number of experimental units required is equal to one less than the sum of the number of blocks and number of treatments. A design in minimal number of experimental units that permits the estimation of all possible pair wise treatment comparisons is called a minimally connected design. The basic problem with the use of minimally connected designs in agricultural experimentation is that they do not provide an estimate of error. Therefore, to get an estimate of error, some modifications in these designs need to be made by adding some more experimental units. Keeping this in view, a catalogue of block designs with $n = v + b - 1 + i$, $i = 1, 2, 3, 4, 5, 6, 7, 8$ has been prepared, where n is the total number of experimental units. Block contents along with lower bounds to A- and D-efficiencies are also given in the catalogue.

Design and analysis of multi-response experiments

Experiments in which data on several responses are measured from an experimental unit corresponding to the application of a treatment are known as multi-response experiments. Multi-response experiments are of two types viz. complete multi-response experiments (all the response variables are recorded from each experimental unit) and incomplete multi-response experiments (recording of all the response variables from each experimental unit is not feasible). For complete multi-response experiments, it has been shown that the designs that are efficient for single response experiments are also efficient for complete multi-response experiments provided the dimensionality of the response vector is smaller than the error degrees of freedom. A stepwise procedure for the multivariate analysis of variance of data generated through block designs for complete multi-response experiments has been developed. To identify the sets of treatments that are significantly different from others, expressions of sum of squares and cross products matrix due to desired treatment contrasts for complete multi-response experiments conducted using block designs have been derived. If two treatments are found to be significantly different in the pair wise treatment comparisons, then we need to identify the better treatment from the two significantly different treatments. A procedure based on J-plot and Euclidean distance of the treatment means has been developed for identification of best treatment in complete multi-response situations.

A method of construction of designs for incomplete multi-response experiments using combination of randomized complete block (RCB) design as treatment-wise design and BIB design as response-wise design has been obtained. The designs obtainable from this method are economical from resource point of view. Stepwise analytical procedure for analysis of data generated from incomplete multi-response designs obtained through above method has also been developed.

Outliers in block designs

An outlier in a set of data is an observation (or an observation vector) that appears to be inconsistent with the remainder of the observations in that data set. Occurrence of outlier(s) is common in every field in which data collection is involved. In agricultural experiments, outlier(s) is/are likely to appear in the experimental data due to disease and/or insect-pest attack on some plots in the field, or due to unintentional heavy irrigation on some particular block(s) or plot(s) of the experiment. Outlier(s) may creep in due to transcription errors. Presence of such abnormally high or low observations may cause a deviation from the assumptions particularly those of normality and homogeneity of observations. It is, therefore, important to detect the presence of outlier(s) along with deviations from these assumptions and suggest remedial measures.

Test statistics have been developed for identification of outlier(s) that takes care of the masking effect and also enables one to detect outliers. Robust methods of analysis based on M-estimation and Least Median Squares (LMS) method have been developed. Designs that are robust in presence of one or two outliers have been identified. Graphic user interface based software has been developed for analyzing experimental data in the presence of outlying observations. The software has the following features: can identify outliers in experimental data; can directly apply the robust methods of estimation viz. M-estimation (Huber's function) or LMS method for analyzing the data and has option to analyze the data after deleting the outlying observations.

A test statistic for detection of a single outlier vector in complete multi-response experiments run in a block design has been developed on the lines of Cook-statistic for single response variable in a block design.

Block designs for test treatments - control(s) comparisons

In practice there may arise experimental situations where it is desired to compare several treatments called test treatments to standard treatments called controls. For example, in screening experiments or in the beginning of a long-term experimental investigation, it is initially desired to determine the relative performance of new test treatments with respect to the existing treatments. Interest may be to study the performance of new types of hybrid varieties, method of cultivation, pesticides, herbicides, etc. and an existing (old) one is to be replaced by one of these newer kinds. The main interest is to compare the new (test) treatments with the old (control) treatment(s) and thus a higher precision is desired for these estimates. For these experimental situations, the usual designs for making all possible pair wise comparisons among treatments may not be efficient. Series of block designs with equal/unequal block sizes for test treatments versus control(s) comparisons have been developed. The problem of making test treatments versus control comparisons when the block effects are random has been investigated. Efficient designs for the experimental settings, (i) where the test versus test comparisons are made with less precision but test versus control comparisons are made with high precision and (ii) when there are several controls and each control has a different importance have been developed. A catalogue of efficient designs is also prepared.

In many experimental situations, for example, in germplasm evaluation trials the genetic material collected from the exploration trips is very limited and the quantity of the seed is not sufficient to have more than one replication of the test treatments. Such experiments are generally conducted using augmented randomized complete block designs. Here, the experimenters would often like to know how many times the control treatments be replicated in each of the blocks so as to maximize the efficiency per observation for making test treatments versus control treatments(s) comparisons. An expression has been obtained for optimum number of replications of the control treatments in an augmented randomized complete block design that maximizes the efficiency per observation. An algorithm for generation of these designs that maximize the efficiency per observation has been developed.

3.2 Row-column designs

When the heterogeneity in the experimental material is present in two directions then row-column designs such as Latin square designs, Youden square designs, generalized Youden designs, Pseudo Youden designs, Youden type designs, etc. are useful. It has been shown that a generalized Youden design under non-regular setting can never be universally optimal. Universal Optimality, E-optimality and Type 1 and Type 2 optimality aspects of row-column designs have been studied. Optimality aspects of structurally incomplete row-column designs with unequal row and column sizes have been investigated. Sufficient conditions for the designs to be simultaneously universally optimal for treatment and column classification have been obtained. General methods for construction of universally optimal structurally incomplete row- column designs have been obtained. A correspondence between structurally incomplete row-column designs, and designs for two stage experiments has been established. This correspondence will go a long way in unifying the research efforts that were made in the literature in two different directions viz. row-column designs and block designs for two disjoint sets of treatments applied in stages or succession. The designs identified are applicable to experimental situations where treatments are to be applied in sequences, particularly in crop sequence, horticultural and animal science experiments.

Semi-Latin squares are useful for situations when the number of levels of both the nuisance factors (factors of heterogeneity) is same and is a factor of number of treatments. Such experimental situations are common in consumer testing, glass house crops, residual effect experiments, sugar beet trials, food industry, etc. A new method of construction of $(n \times n)/2$ semi-Latin squares has been obtained.

For comparing several test treatments with control treatment(s), efficient row-column designs and structurally incomplete row column designs have been obtained.

3.3 Block designs with nested factors

Nested block designs

A nested block design is defined as a design with two systems of blocks such that the second system of blocks is nested within the first system of blocks. These designs are quite useful in many experimental situations. For example, consider a field experiment conducted using a block design and harvesting is done block wise. Harvested samples are to be analyzed for their contents either by different technicians at same time or by a technician over different periods of time. The variation due to technicians or time periods may be controlled by another blocking system. Technicians or time periods form a system of blocks that are nested within blocks. Such experimental situations are also common in post harvest value addition of horticultural and vegetable crops. Nested block designs are also quite useful in agricultural field experiments where the plots with similar fertility occur in patches rather than in a uniform direction. Nested balanced incomplete block (NBIB) designs are useful for these situations. In a NBIB design, block classification ignoring sub-blocks is a BIB design and sub-block classification ignoring blocks is also a BIB design. A complete catalogue of NBIB designs with number of replications $r \leq 30$ has been prepared. The catalogue contains a total of 299 designs. Out of 299 designs, 8 designs are non-existent. A new method of construction of NBIB designs has been obtained. Using this method and trial and error solutions, block layouts of 22 new NBIB designs have been obtained. The layout of 199 designs with block contents has been prepared. The solution for the block layout of remaining 92 designs is unknown and the statisticians need to develop methods of construction of these NBIB designs. The designs catalogued have also been identified for 1-resolvable and 2-resolvable sets.

A NBIB design may not exist for all parametric combinations or even if it exists may require a large number of replications, which the experimenter may not be able to afford. To deal with such situations, nested partially balanced incomplete block (NPBIB) designs have been introduced in the literature. Some new methods of construction of NPBIB designs based on group divisible association scheme have been obtaned. Catalogues of NPBIB designs based on 2- associate and 3- associate class association schemes have been prepared. Universal optimality aspects of non-proper block designs with nested rows and columns have been studied. Some general methods of construction of optimal designs under this setup have also been given.

A β-version of the software for generation of efficient nested block designs has been developed. It consists of 3 modules viz. (i) nested block designs with independent observations; (ii) nested block designs when the observations within a sub-block have a nearest neighbour correlation structure and (iii) nested block designs when the observations within a sub-block have a nearest autoregressive correlation structure. Once the number of treatments (v), number of bigger blocks (b), bigger block size (k), number of sub-blocks nested within a block (q) and the value of correlation coefficient (r) is entered (in case of correlated observation), the design gets generated.

Nested block designs for making test treatments-control treatment comparisons

Nested block (NBIB and NPBIB) designs are useful for experimental situations where the experimenter is interested in making all possible pair wise treatment comparisons with as high a precision as possible. However, there do occur experimental situations where the experimenter is interested in comparing several new treatments with existing practice with high precision and the comparisons among the test treatments are not of much importance. To deal with such situations, nested balanced treatment incomplete block (NBTIB) designs have been introduced. Some new methods of construction of NBTIB designs making use of NBIB designs, initial block solutions, etc. have been developed. A method of construction of nested block designs for making test treatments-control treatment comparisons has been developed which yields minimally connected designs with respect to sub-blocks. The design with respect to bigger blocks is a group divisible treatment design.

Doubly nested block designs

Nested block designs are useful for experimental situations with two sources of variation in the experimental units, one nested within another. There may, however, arise a situation when there exists another source of variation among the units in sub-blocks of an incomplete block design. Consider a field experiment which is conducted at several locations using a nested block design where locations are taken as blocks and harvesting time is taken as sub-blocks. But harvested samples from each sub-block are to be analyzed for their content in laboratory by different technicians. To control variation due to technicians, this may be taken as another blocking factor. Hence, nesting of units within sub-blocks may be required. Doubly nested incomplete block designs are useful for such situations. An exhaustive catalogue of doubly nested balanced incomplete block (DNBIB) designs for number of treatments $v \leq 20$ and $r \leq 20$ is available in the literature. A DNBIB design may not exist for all parametric combinations or even if it exists, may require large number of replications which the experimenter may not be able to afford. To deal with such situations, a new class of designs called doubly nested partially balanced incomplete block (DNPBIB) designs has been introduced. Some general methods for construction of DNPBIB designs are obtained using DNBIB designs, NBIB designs and PBIB designs.

Block designs with nested rows and columns

For the experimental situations where there are two cross-classified factors causing heterogeneity in the experimental material and are nested within the blocking factor, block designs with nested rows and columns have been introduced. Several methods of construction of designs with nested rows-columns (BIB-RC designs) have been developed and a comprehensive catalogue of BIB-RC designs has also been prepared. Universal optimality aspects of non-proper block designs with nested rows and columns have been investigated. Some general methods of construction of optimal block designs with nested rows and columns have been obtained and a catalogue of universally optimal designs has been prepared. Some methods of construction of block designs with nested rows and columns that are optimal according to Type 1 criterion have also been obtained.

Efficient block designs with nested rows and columns for making test treatment-control treatment(s) comparisons have also been obtained.

3.4 Computer aided search of efficient designs

In the literature on design of experiments, methods of constructing optimal designs are given for various experimental settings. However, these methods do not give flexibility to obtain an optimal/efficient design for any desired parametric combination in a given experimental situation. This limitation can be overcome by using intelligent computer algorithm. Computer algorithms for generation of efficient designs based on exchange and interchange procedures have been developed. The procedure of computing lower bounds to A- and D-efficiencies has been incorporated in the algorithms. Several new efficient designs for making all possible pairwise treatment comparisons have been obtained. Efficient designs for the parametric combinations for which BIB designs are non-existent or solutions are unknown have also been obtained. Efficient designs for making test treatments-control treatment(s) comparisons with differential precision have been obtained through the computer aided search. The computer algorithms have also been modified and implemented for obtaining efficient designs under correlated error structures for (i) block designs for making all possible pairwise treatment comparisons; (ii) block designs for making test treatments-control treatment comparisons; (iii) nested block designs and (iv) cross over designs. Algorithms for construction of efficient α-designs have also been developed using exchange and interchange procedures.

3.5 Block designs for correlated observations

One of the requirements in the analysis of data from designed experiments is that the observations should be independent. But, there may arise situation when the observations are correlated. In agricultural field experiments, usually the fertility levels are changing over space. Plots occurring close together within a field area are more similar than plots occurring far away from each other. Thus, the observations from the neighbouring plots are likely to be correlated. The observations may be correlated because of the layout of the plots, pest infections from neighbouring plots or some local factors which blocking cannot remove. In industrial experiments, suppose only a certain number of experimental runs can be made during a particular time period such as a plant shift or a day. Here, time contiguity is used as criterion of blocking and there may exist correlation within the time block caused by the equipment ageing and wear out. In this situation, it is desirable to obtain designs and perform analysis in which the correlations are taken into account. Catalogues of efficient block designs and nested block designs for making all possible pair-wise treatment camparisons under nearest neigbour and auto correlated error structures have been prepared. A catologue of efficient block designs for making test treatments-control treatment comparisons and change over designs under autoregressive correlated error stuructures has been prepared. Series of pair-wise uniform incomplete block designs under this situation have been obtained.

3.6 Block designs with neighbour effects

In agricultural field experiments, it may so happen that the treatment applied to one plot in a block may affect the response on the neighbouring plots if the blocks are formed using adjacent plots with no gaps. Neighbour balanced block (NBB) designs have been defined to ensure that no treatment is unduly disadvantaged by its neighbour. Some series of balanced/ partially balanced and complete/

incomplete NBB designs have been obtained. Optimality aspects of block designs with neighbour effects under fixed and mixed effects model have been studied. Some series of NBB designs for comparing a set of test treatments to a control have been developed. The designs obtained are totally balanced in the sense that all the contrasts among test treatments for direct, left and right effects are estimated with same variance and all the contrasts pertaining to test versus control for direct, left and right effects are estimated with the same variance. The concept of NBB designs has been defined for the experimental situation where the treatments are the combinations of levels of two factors and only one of the factors exhibits neighbour effect. Some methods of constructing complete NBB designs for two factors (useful in agroforestry experimets) neighbour balanced for one factor have been obtained. These designs are variance balanced for estimating the direct effects of contrasts pertaining to combinations of levels of both the factors. An incomplete NBB design for two factors has also been given which is found to be partially variance balanced with three associate classes. Several methods of construction of serial designs have been obtained and the analytical procedures have been developed using the linear model accommodating the left and right neighbour effects on each treated plot. Several methods of construction of complete as well as incomplete block designs have been obtained by making use of the directed graphs and factorial structure. An analytical procedure for the analysis of these designs under the assumption of (i) equal left and right neighbour effects and (ii) no competition effect of a treatment with itself has also been developed. The performance of a series of incomplete NBB design for autoregressive [AR(1)] and nearest neighbour (NN) error correlation structure is studied when generalized least squares estimation is used. The designs with AR(1) structure turns out to be more efficient and the efficiency of direct effects of treatments is more as compared to neighbour effects under both the structures.

4. Multi-factor Experiments

The theoretical developments in experimental designs at IASRI began with obtaining confounded designs for asymmetrical factorial experiments in 1950’s. Since then a lot of developments have taken place in multi-factor experiments. Some of these are described in the sequel.

4.1 Confounded designs for asymmetrical factorial experiments

Several efficient confounded designs for asymmetrical factorial experiments have been obtained using the technique of collapsing and replacement and a catalogue of efficient designs have been prepared.

Balanced confounded factorial experiments for symmetrical as well as asymmetrical factorial experiments, providing flexibility in the choice of factors and their levels have been constructed. Procedures of analyzing these designs have also been suggested.

4.2 Designs for crop sequence experiments

Equivalence between extended group divisible (EGD) designs and designs for crop sequence experiments has been established. This equivalence has encouraged the agricultural experimenters in the use of EGD designs for their experimentation. This equivalence is also useful for the experimental situations where the blocking criteria are implemented in succession and there is likelihood of the interaction effect between the direct effects and residual effects of the treatments applied at two successive stages. Some new methods of construction of EGD designs have been obtained and a catalogue of these designs with a maximum of 5 replications has also been prepared.

4.3 Fractional factorial plans

For screening experiments or when the higher order interactions are negligible or the experimental resources are not enough for one complete replication, fractional factorial plans and particularly orthogonal resolution plans have been obtained. A new method of construction of confounded designs for fractional asymmetrical factorial experiments has been developed. This method is quite general and is applicable to the symmetrical factorial experiments as well. Some series of resolution III plans for asymmetrical factorial expriments have been constructed. Orthogonal resolution IV plans for asymmetrical factorials have been obtained. Two series of designs for 3×2^n and 5×2^n experiments are constructed. General class of main-effect plans for $3^m\times2^n$ experiments has been proposed. These plans are irregular fractions, and have been constructed with the help of BIB designs. They are generally non-orthogonal in nature. A complete catalogue of orthogonal main effect plans has been prepared. A new exchange algorithm (EA) for construction of D-optimal designs was developed. This EA uses D-optimality criterion and can be applied in the settings of fractional factorial plans). This EA is used to construct 54 D-optimal 2^m fractional factorial plans of resolution V for m = 4, 5 and 6. D-optimal saturated main effect plans for three factors when the first factor is at three levels have been obtained using a computer algorithm.

Several methods of construction of symmetric and asymmetric orthogonal arrays have been obtained. Resolvable orthogonal arrays have been used in construction of fractional factorial plans. Some methods of obtaining resolvable (symmetric) orthogonal arrays and resolvable mixed orthogonal arrays have been given. The methods are derived from the use of Kronecker Product and Kronecker sum of matrices.

4.4 Supersaturated designs

In industrial, biological and agricultural experiments, there occur experimental situations where a large number of factors are to be tested but only few of the factors are active. In such experiments, the experimenter's endeavour is to minimize the number of runs to identify the active factors for efficient utilization of resources and minimization of cost and time. Supersaturated design (SSD) is a fractional factorial plan whose run size is not large enough for estimating the mean and all the main effects. The main attraction for using SSDs is their run size economy. SSDs for two-level, multi-level and mixed level factorial experiments have been obtained using resolvable orthogonal arrays; Hadamard matrices and proportional frequency plans. Some criteria for comparing SSDs for asymmetrical factorial experiments and/or unbalanced designs are given. A column-wise co-ordinate exchange algorithm for generation of SSDs for two-level, multi-level and mixed level factorials has also been developed.

4.5 Response surface designs

The above discussion relates to the experiments in which the levels or level combinations of one or more factors are treatments and the data generated from these experiments are normally analyzed to compare the level effects of the factors and also their interactions. Though such investigations are useful to have objective assessment of the effects of the levels actually tried in the experiment, this seems to be inadequate, especially when the factors are quantitative in nature and cannot throw much light on the possible effect(s) of the intervening levels or their combinations. In such situations, it is more realistic and informative to carry out investigations with the twin purposes:

a) to determine and to quantify the relationship between the response and the settings of a set of experimental factors, and

b) to find the settings of the experimental factor(s) that produces the best value or the best set of values of the response(s).

If all the factors are quantitative in nature, it is natural to think the response as a function of the factor levels and data from quantitative factorial experiments can be used to fit the response surface over the region of interest. The special class of designed experiments for fitting response surfaces is called response surface designs. Second order rotatable response surface designs (SORD) have been obtained through BIB designs. The concept of group divisible rotatable response surface designs has been introduced. Second order rotatable and group divisible rotatable response surface designs have been obtained for 4 level and 6-levels factorial experiments. The rotatable designs for asymmetric factorial experiments have been introduced using the transformation of levels of rotatable designs for symmetrical response surface designs.

Method of construction of SORDs with blocking has been obtained. The blocking of the SORD satisfying the condition of orthogonal blocking usually requires a large number of experimental points. However, if one of the requirements of orthogonal blocking is waived, the problem of blocking becomes somewhat easier and the size of the experiment in such a case can be greatly reduced. Though in such designs, surface parameters are not all free from block effects.

Some modified and/or rotatable response surface designs useful for response optimization for symmetric as well as asymmetric factorials with equispaced doses have been obtained. Some efficient response surface designs for slope estimation for symmetrical factorials with equispaced doses have also been obtained using MINIMAX criterion. A catalogue of modified and/or rotatable response surface designs with orthogonal blocking is also prepared. Modified and rotatable second order response surface designs developed have been used by the Division of Agricultural Engineering and Division of Post Harvest Technology, IARI, New Delhi and Division of Biotechnology, IVRI, Izatnagar.

The problem of selecting explanatory variables for the case of non-linear models has also been investigated. The design criterion heavily depends on initial guess of the parameters in non-linear set up. The criterion of D-optimality is used for selecting any design. Replication structure of the experiments under a non-linear set up has been examined. Replicating all the basic design points equally gives increased valued of the criterion. A sufficient condition for a replicated design to be optimum is provided.

First and second order response surface models with neighbour effects from immediate left and right neighbouring units have been considered and the conditions for the estimation and rotatability of these models have been derived. Response surface methodology in the presence of neighbour effects as well as correlated error structure has been developed. Designs for fitting response surface models with quantitative-cum-qualitative factors have been studied under neighbour effects/ correlated error structure.

In several response surface designs, data on several response variables is recorded. Such experimental situations are common in food processing experiments. The experimenter is interested in obtaining a combination that simultaneously optimizes all the response variables. A procedure of estimation of parameters from linear multi-response models for incomplete multi-response experiments has been developed. Procedure of simultaneous optimization of complete and incomplete multi-response experiments has been developed and SAS codes are developed for its implementation.

4.6 Experiments with mixtures

There do occur experimental situations where a fixed quantity of inputs, may be same dose of fertilizer, same quantity of irrigation water or same dose of insecticide or pesticide etc. are applied. The fixed quantity of input is a combination of two or more ingredients. For example, fixed quantity of water may be a combination of different qualities of water sources or fixed quantity of nitrogen may be obtained from different sources. In a pesticide trial, a fixed quantity of pesticide may be obtained from four different chemicals. In these experiments the response is a function of the proportion of the ingredient in the mixture rather than the actual amount of the mixture. The experiments with mixture methodology are quite useful for these experimental situations. Experiments with mixtures methodology will give a functional relationship between proportions of inputs applied and response and is helpful to interpolate responses at points that have not been tried in the experiment. Optimum combination of proportions can also be obtained through this approach.

In some experimental situations it may not be possible to explore the total range of all the components because one may require that at least a certain amount of a particular component may be present in all blends or one may insist that the proportion of component may not exceed a certain proportion. Such constraints give lower and/or upper bound on different components of mixtures. In certain experimental situations there may be one or more factors that are not component(s) of the mixture but influence the response. This type of factor(s) is(are) called process variable(s). A method of construction of restricted region simplex design in the presence of process variables when upper bound is imposed on one of the components of the mixture has been obtained using response surface designs with equispaced doses. Extreme vertices algorithm has also been developed for obtaining designs with restricted regions. The designs for experiments with mixtures with orthogonal blocking have also been obtained.

There do occur many experimental situations, wherein designs for multi-factor mixture experiments are required. Designs for multifactor mixture experiments available in literature are useful for fitting only the first order model for two factor mixture experiments only. In agricultural experiments, behaviour of different ingredients may be quadratic in nature, therefore, multifactor designs for experiments with mixtures need to be obtained so as to fit the second order response surface for multifactor mixture experiments. Designs for multi-factor mixture experiments have been obtained using response surface designs and projection matrices.

5. Some Other Considerations

5.1 Designs for biological assays

In a biological assay, a test (new) preparation and a standard one are compared by means of reactions that follow on their applications to some subjects. Characterizations of designs for symmetrical and asymmetrical parallel line assays have been obtained and methods of construction of designs satisfying these characterizations have been generated. These designs are generally simple partially efficiency balanced designs because of the nature of the contrasts of interest. The contrasts on interest need to be estimated with full precision.

Efficient designs for symmetrical parallel line assays that estimate all the three contrasts of interest with as high a precision as possible have been obtained and catalogued. Some methods of construction of symmetric multiple parallel line assays and slope ratio assays have also been obtained.

5.2 Designs for microarray experiments

Microarray experiments are conducted to study the relative expression levels of thousands of genes simultaneously and identification of differentially expressed genes. Work on design and analysis of microarray experiments was initiated and optimality aspects of designs by taking array, dye and variety effects in the model has been studied. Lower bounds to A- and D-Efficiencies have been obtained under mixed effects model taking array effects as random. Algorithm has been developed for obtaining efficient block designs for micro array experiments. Designs that are efficient for both the situations when array effect is taken fixed and as well as random effects have been identified. Analytical procedures based on mixed effects model considering array effects as random has been developed for identification of differentially expressed genes.

5.3 Designs for two-line and four line cross experiments

Optimal proper and non-proper incomplete block designs for diallel cross experiments for the estimation of contrasts among the general combining ability effects have been obtained and catalogued. Optimal balanced augmented block designs for diallel crosses have also been obtained and catalogued. Efficient partial diallel cross plans have been obtained from the three-class association schemes and a catalogue of these plans has been prepared. Optimal block designs for diallel crosses for estimation of heritability and ratio of variance components have been obtained to deal with the experimental situations in which the parental lines are randomly selected from a population of lines.

5.4 Block designs for multistage experiments

In experiments where the experimental unit is long lived, for example, horticultural experiments with trees as experimental units, different sets of treatments may be applied at different stages of the growth of tree. Other experimental situations like this could be experiments using animals as units. Such designs are known as multi-stage designs with two (or more) sets of non-interacting (or may be interacting) treatments. To deal with such experimental situations, block designs for two interacting / non-interacting sets of treatments applied in succession have been developed. Through these designs, the comparison among the direct effects of the treatments applied at second stage and residual effects of the treatments applied at the first stage can be made. A correspondence has been established between structurally incomplete row-column designs, block designs with nested rows and columns and designs for two stage experiments.

5.5 Cross over designs

Experiments with biological entities, like trials with animals, often involve application of a sequence of treatments to each experimental unit over varying periods of time using crossover designs (CODs). When experimental units exhibit larger variability or when the number of units is limited due to ethical or cost reasons, a COD allows treatments to be adequately replicated. In the literature, these designs are known by many other names *viz.*, repeated measurements designs, change over trials, switchover trials, designs involving sequences of treatments, time-series designs, before-after designs, *etc*. These designs are used advantageously in nutrition experiments with dairy cattle, clinical trials in medical research, psychological experiments, long-term agricultural field experiments, bioequivalence trials, *etc*. The peculiarity of a COD is that any treatment applied to a unit in a certain period influences the responses of the unit not only in the period of its application but also leaves residual effects in the following periods.

The residual effects may persist for one or more periods. Generally a blank period is left for washing away the effect of the treatment in the previous period.

CODs can be classified on the basis of the properties they possess. We present a brief account of such classifications along with the contributions made by division of Design of Experiments.

A COD is said to be uniform over periods (experimental units), if each treatment occurs equally often in each period (experimental unit). A COD is said to be uniform if it is uniform over both periods as well as units.

Pre-period or 0^{th} period is a period preceding the first experimental period in which appropriate treatments are applied to the experimental unit but either the observations are not recorded or if recorded they are not taken into consideration while carrying out the analysis of the data. By adding a pre-period to the design, the first period observations also receive the residual effects of the treatments and hence the data become homogeneous. A COD allowing the estimation of direct and first residual effects with one pre-period, in which the treatments in the period are exactly the same as those in the last period, is called a circular COD.

CODs in which every treatment is preceded equally often by every other treatment in the sequences have been called combinatorial balanced with respect to first order residual effects. A design is said to be strongly balanced if each treatment is preceded by every treatment including itself equally often. A COD permitting the estimation of first order residual effects is called variance balanced if the variance of any elementary contrast among the direct effects is constant, say α, and the variance of any estimated elementary contrast among the residual effects is also constant, say β. Here α and β may not be equal. If $\alpha = \beta$, then these designs are known as totally balanced COD.

The work at IASRI on CODs was started with the problem of construction of CODs having incomplete periods, balanced for first order residual effects of treatments. A simple method of construction of William square designs balanced for first order residual effects of treatments has been developed at the Institute. A catalogue of CODs requiring only 50 or less experimental units have been prepared that serves as a ready recknoer for the experimenters.

Universal optimality aspects of CODs when number of periods is less than number of treatments has been investigated and sufficient conditions have been obtained for a COD to be universally optimal in a pre-defined class of designs. Optimality aspects of some series of CODs in the presence of first and second order residual effects have also been investigated. Series of balanced CODs, optimal in a given class of designs has been obtained.

Series of CODs balanced for first as well as second order residual effects have been obtained. Two classes of totally balanced designs have been obtained considering the presence of first order residual effects of treatments.

A minimal balanced design contains the minimum possible number of experimental units. A general method of construction of minimal balanced CODs for odd number of treatments along with an outline of their analysis has been given. Further, two new classes of minimal strongly balanced CODs assuming the presence of first order residual effects has been obtained. These designs are partially variance balanced with *m*-associate classes based on a circular association scheme. A class of cyclic CODs has been obtained.

Circular CODs have been obtained by associating circular designs with a complete set of mutually orthogonal Latin squares.

A method of constructing completely balanced CODs that permit the estimation of direct effects orthogonal to all other effects, when the residual effects of treatments last for two consecutive periods, has been developed. Some methods of construction of partially balanced CODs have also been given. A series of ternary CODs along with a method of analysis has been proposed. The assumption in these designs was that in a given sequence a treatment should not occur more than two times and the same treatment should not appear in two consecutive periods.

Designs that give independent estimates of direct and residual effects, of approximately equal precision, are obtained by adding an extra period to the original design. In the new final period, the treatments that were applied in the previous final period are repeated. Some series of extra-period CODs have been obtained.

The performance of two-treatment CODs in the presence of time trends has been studied. The efficiency of estimation of various treatment effects of two-treatment CODs has been improved by adding a pre-period with appropriate treatments. Some efficient two-treatment CODs when the errors are auto-correlated has been obtained.

The combinatorial aspects of CODs for making test treatments- control treatment comparisons have been studied. Schur optimality aspects of CODs for comparing several treatments with a control have been studied. It has been shown that the Schur-optimal control CODs are necessarily balanced. Some methods of construction of Schur-optimal balanced control CODs have been given.

In many agricultural experiments and veterinary medical trials, it is often required to measure the effect of response from simultaneous application of levels of two or more factors over varying periods where levels of at least one factor exhibit residual effects. An amalgamation of CODs and factorial experiments may be required in such situations. Two-factor symmetrical split-type CODs have been developed. Two classes of uniform strongly balanced CODs with two factors balanced for residual effects of levels of one factor have been obtained. For situations where the two factors are unrelated but existence of first order residual effects of both the factors are suspected, CODs with two non-interacting factors assuming residual effects to be present have been obtained using mutually orthogonal Latin squares and William squares.

Almost all the studies have been carried out under the assumption that observations are independent but two successive observations can have a correlation structure. The necessary and sufficient conditions for designs to be balanced in presence of auto-correlated errors have been obtained. In a COD, a sequence of treatments is applied to an experimental unit and observations are recorded over the periods and hence it is very much possible to observe interaction between treatments and experimental units. A non-additive model with treatment $\times$ unit interaction effects is recommended for such situations, as these effects also contribute significantly to the response measured. Under a non-additive model, a uniform balanced non-circular class of CODs with a pre-period has been shown as universally optimal for the estimation of direct effects.

In general, the effects in the COD model are considered as fixed and observations are uncorrelated and distributed normally. Many a time the assumptions made in the model are violated and have an effect on the estimates of treatment contrasts. Hence, variance of treatment contrasts, when the unit effects are considered as random and the observations are correlated and/or non-normally distributed, have been estimated through simulation studies. An attempt has been made to study the efficiency of treatment comparisons using Bayesian analysis, empirically. It was seen that the estimate obtained under Bayesian approach using GIBBS Sampling (BUGS) is much smaller than that obtained under classical approach for the same data set.

CODs have immense applications in bioequivalence trials. Bioequivalence refers to the degree to which clinically important outcomes subjected to a new preparation resemble those of a previously established preparation. Standard CODs are being used in bioequivalence trials, but they treat all pair-wise comparisons of formulation effects with equal importance. The experimenters are more interested in the comparison of several test formulations to an established standard or control or reference formulation rather than in all pair-wise comparisons. Some series of reference balanced CODs for bioequivalence trials with or without considering residual effects have been obtained.

5.6 Robust designs

It has been described in section 2 that robustness of designs may be investigated against disturbances or accidents like loss of data, interchange or exchange of treatments, presence of a systematic trend among observations in a block, presence of outliers, etc. The criterion of robustness against any of these disturbances could be in terms of connectedness of design, variance balance, optimality, orthogonal factorical structure, trend free, efficiency of the residual design after the accident, etc. The robustness of designed experiments has been studied under a general linear model for inferring on a set of treatments as per the connectedness criterion as well as the A-efficiency criterion. It has been shown that a design robust under a homoscedastic set up is also robust under the general heteroscedastic set up with correlated observations. The robustness of block designs has been studied in particular against the loss of data, in general against loss of any t observations. Designs robust against the loss of one, two and three observations have been identified. Robustness of block designs against the loss of any two blocks, not necessarily disjoint, has also been studied. Similarly, the robustness of row-column designs has also been investigated against the loss of data. The resistance of variance balanced block designs with unequal block sizes that are universally optimal has been investigated against the loss of all the observations pertaining to a treatment. Some methods of construction of resistant designs have also been obtained. Binary variance balanced block designs have been shown to be robust against (i) missing observations; (ii) exchange of a treatment; (iii) interchange of a pair of treatments and (iv) presence of one or two outlier(s). Several diagnostic criteria for detection of outliers in experimental data have been developed. Robustness aspects of designs against the presence of one outlier have been investigated. It has been shown that all BIB designs and binary balanced block designs are robust in presence of two outliers. All other E-optimal designs are robust in presence of one outlier. Several 2-associate class PBIB block designs and variance balanced row-column designs that satisfy the property of adjusted orthogonality, nested balanced incomplete block designs have been shown to be robust in presence of a single outlier.

Balanced treatment incomplete block designs have been identified that are robust against the presence of any one of the following disturbances (i) one observation missing, (ii) one block missing, (iii) exchange of a treatment, (iv) interchange of a pair of test treatments, and (v) presence of a single outlier. Balanced bipartite block designs that are resistant against the loss of all observations pertaining to a test treatment have been introduced.

Robustness of neighbour balanced designs has been investigated against loss of data and also for different correlation structures and against different values of correlation coefficient.

Binary balanced block designs for diallel crosses have been shown to be robust against the presence of any one of the following disturbances (i) exchange of a cross, (ii) interchange of a pair of crosses, (iii) single observation missing, (iv) all the observations pertaining to a block missing, and (v) presence of a single outlier.

It is well known that an EGD design, if exists, has the property of Orthogonal Factorial Structure with balance. During the course of the investigation, a particular level of some factor turns out to be lethal resulting in the loss of all the observations pertaining to treatment combinations with this level of factor. High cost or non-availability of inputs may sometimes force the experimenter to discard such observations and continue with the experimentation. Such kind of exigencies may disturb the original structure of the design. Thus the concept of structure resistant designs has been introduced at IASRI for the first time. The designs retain the property of orthogonal factorial structure with balance when all the observations pertaining to the treatment combinations containing one level of a particular factor are lost. Robustness aspects of designs for such situations have been studied and structure resistant designs have been obtained.

For multi factor experiments, sometimes level of a particular factor may be lethal or experimental material pertaining to this level of the factor could not be procured in time and as such all the observations pertaining to the treatment combination containing that level of the particular factor are lost. Robustness aspects of designs for such situations have been studied and structure resistant designs have been obtained.

Robustness aspects of response surface designs against single missing observation have been investigated using efficiency per obsevation criterion.

Robustness of designs for bioassays against the loss of a dose has been investigated. The loss of all the observations corresponding to a dose (standard or test) gives rise to designs for asymmetric parallel line assays. This is another example of structure resistant designs. Using the structure resistance property, several designs for asymmetric assays have been obtained.

Robustness aspects of CODs have also been investigated against missing observation(s) using efficiency criterion. CODs balanced with respect to first order residual effects were found to be robust against the loss of observation(s) from one experimental unit.

In some experimental situations, there may exist a systematic trend in the experimental units. Designs that allow the estimation of contrasts of interest free from trend effects are known as trend free designs. Conditions for a BIB design, NBIB design and proper binary variance balanced block design for diallel crosses to be trend free have been obtained and catalogues of trend free BIB designs, NBIB designs and proper binary variance balanced block designs for diallel crosses have been prepared for the benefit of the experimenters.

Systematic trend may also be present in the experimental units while conducting a factorial experiment. If there is trend in the experimental units, the interest of experimenter is to eliminate the trend effect and obtain the estimates of contrasts of interest (main effects and lower order interactions) free from trend effects. The resulting designs are called as trend-free designs for factorial experiments for the effects of interest and ordered application of treatments to experimental units is called run order. Computer aided search has been made for linear trend-free designs for 2-level factorial experiments both with and without confounding. Computer aided search has also been made to identify the two-factor and three factor interactions that can be estimated free from trend effects along with main effects. Computer aided search has also been made to obtain fractional factorial plans that provide the estimates of main effects free from block effects.

In a CODs also, observations are taken over periods from experimental units and hence it is quite possible that the units exhibit trend over the periods. Validity of least square technique for the analysis of CODs balanced for first and second order residual effects of treatments when the experimental units exhibit time trends over periods has been investigated. A class of two-period totally balanced trend-free CODs in the presence of first residual effects that allow the estimation of treatment effects orthogonal to trend effects has been developed.

5.7 Sampling vis-à-vis design of experiments

The use of interesting combinatorial properties of binary, proper block designs like balanced and doubly balanced incomplete block designs, partially balanced incomplete block designs, cyclic designs, etc. enables one to generate inclusion probability proportional to size sampling schemes for sample size more than two. The sampling schemes are easy in operation. The ease in sample selection is achieved by building an association between sampling design and the experimental design. The experimental design is mapped onto the sampling design. The treatments (v) are the population units (N), the totality of the blocks is the sample space (S containing b samples), the sample size (n) is the block size (k) and the contents of a block are the sampled units. In this respect the sampling scheme is very simple in operation. A probability measure is defined on the sample space. The selection of one block with a pre-assigned probability gives the entire sample. The sampling schemes so generated are in fact controlled selections in the sense that only a subset of all the possible samples of size n has a non-zero probability of selection while all the remaining samples have a zero probability of selection. As the choice of design is not unique, the desired precision of estimation can also be achieved by controlling the second order inclusion probabilities. Many sampling schemes have been generated by this technique.

For estimating the variance of nonlinear statistics like regression and correlation coefficients, birth and death rates, from a complex survey data, the method of balanced repeated replication is more useful than the other methods like linearization, bootstrap and jackknife repeated replications. Once again a relationship is established between mixed orthogonal arrays of strength two and the balanced repeated replications. This relationship has enabled to draw samples with unequal number of selections per stratum. The use of proportional frequency plans as balanced repeated replication has also been exploited by adjusting for bias. A bias corrected non-linear statistic is also obtained. Based on simulation studies, it has been shown that the proposed method is better than the grouped method.

Design combinatorics and linear programming approach have been exploited in generating balanced sampling plans for sampling from populations in which adjacent units provide similar observations due to natural ordering of units in time or space. An algorithm for generation of balanced sampling plans excluding adjacent units (BSA plans) has been developed. A new family of distance balanced sampling plans (DBSP) with the property that the second order inclusion probabilities are non-decreasing function of distance between the two concerned units is developed. Inclusion probability propertional to size sampling plans excluding adjacent units have been developed by making use of binary, proper and unquireplicated block designs.