TREATMENT DESIGN DEFINITIONS, TYPES, and PROPERTIES

by

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Abstract

One of the most important aspects of any scientific investigation involving the collection of data is the selection of the entities (treatments) for the investigation. The selection of the treatments for the experiment is known as the treatment design. The success of any investigation depends heavily upon the selection of treatments for the experiment. Because of the great importance of treatment design in experimentation considerable thought should be devoted to this aspect of scientific investigation. Much of treatment design lies outside the field of Statistics. However, there is a considerable part of treatment design that involves statistical considerations. This aspect of treatment design is considered in the present paper.

All absolute and comparative experiments are divided into six types as follows: Controls, one factor, two or more factors, genetic, nested or hierarchical, and bioassay. Relationships among the various types are noted. The properties discussed are balanced confounding or "order-balance," pairwise balance, and a number of properties related to fractional replication such as regular and irregular, balanced resolution V, invariance, semi-invariance, aliasing structure, optimality, and variance optimality. The procedures for selecting treatments for uni-stage or multi-stage experiments, for sequential experimentation, based on previous results of treatments, and for augmentation are discussed to a limited extent. It is noted that these are procedures and not properties.

A thorough study of the subject of treatment design is of pressing importance. Precise definitions, formulations, characterizations, ramifications, and equivalences are needed. Such a study will serve as an aid to the selection of a treatment design and will pave the way for developing new properties for treatment designs. The present study is a first step in this direction.

Treatment Design Properties, Types, and Definitions

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1. INTRODUCTION

As was indicated in the discussion of experiment design (the arrangement of treatments in an experiment) in BU-394-M, there are also many unsolved problems associated with treatment design (the selection of the treatments in an experiment). A classification of the various types of treatment designs and definitions and a description of some of the properties and unsolved problems associated with treatment designs are presented in the present report.

Sir Ronald A. Fisher and others (see BU-394-M) put forth principles and properties of experiment design but comparable results are not available for treatment design. However, Yates [1937] does give a number of definitions associated with the factorial treatment design. In the following we shall classify and define other types of treatment design in a similar fashion and present a somewhat unified discussion of the subject.

The goals of the investigator may be achieved in one or more ways and by one or more treatment designs. In certain cases, the experimenter may wish to estimate main effects and interactions, he might wish to describe a response surface, or he might wish to do both simultaneously. Depending upon what the experimenter wishes to do, a complete or a partial factorial treatment design might be selected. Thus, a response surface study is not to be considered as a treatment design but rather as a goal of the experimenter. Either a partial factorial or a complete factorial treatment design may be used to describe a response surface.

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Many treatment designs could be considered as partial or complete factorial treatment designs. Instead of trying to broaden Yates' [1937] definition of a factorial treatment design and to place all treatment designs under this category, the various types of treatment designs are discussed and their relationships noted. In particular, the following types of treatment design are discussed in the next section:

(i) controls included or not.

(ii) one factor at several levels.

(iii) two or more factors each at several levels.

(iv) genetic (many of these could have been placed under the other categories.)

(v) nested or hierarchical.

(vi) bioassay.

In section three, various properties of treatment designs are discussed. In the fourth section, procedures of using treatment designs are discussed. A few general unsolved problems are given in the last section.

2. TYPES OF TREATMENT DESIGNS AND SOME DEFINITIONS

2.1. Controls included or not in the experiment.

In many experiments a reference point is needed in order to answer or to obtain evidence for a number of questions. A check treatment, a standard treatment, a control treatment, a dummy treatment, or some other designation of a reference point treatment or treatments is often included. In medical experiments a placebo, which is a medical treatment alike in all other respects except that the active ingredient for the infection or disease is not included, or several placebo types are often necessarily included in order to obtain a reference

point(s) for comparisons. Inadequate types of controls in experiments usually decrease the value of the experimental results, even to the point of making the entire experiment only an experience.

One or several control treatments may need to be included in each of the following types of treatment designs. This may be necessary in order to obtain information on comparisons required by the experimenter.

In addition to the controls in an experiment, a number of other treatments may be included in an experiment. These additional treatments constitute a treatment design fitting one of the following five types. The selection of controls is an item by itself just as is the selection of the remaining treatments. For this reason, the selection of the controls in an experiment is considered to be a separate entity.

2.2. <u>One factor at several levels</u>.

In many types of experimental investigations, information is desired for the limited situation in which only one variable or factors affecting the response in the experiment are held constant, are measured, or are ignored. Thus, information is required on the variable X_i, $i = 1,2,\ldots,n$. The values of i may be pre-selected or they may occur from a random sample of the i subscript variable. In experimentation, it would be desirable for the total X-space (the total space over which the variable is defined) to be precisely defined. In discussing properties of treatment designs,it is essential that the X-space, or the total range for the X variable, be precisely defined.

The selection of the different levels of the variable X is dependent upon the nature of the response function, i.e., $Y_{ij} = f(\underline{\beta}, X_i, \epsilon_{ij})$ where $\underline{\beta}$ = a p x 1 vector of parameters, $p = 1,2,\ldots$, $j = 1,2,\ldots,r_i$, X_i represents the values of the variable X, and ϵ_{ij} represents a random error component. If the form of the function is

unknown then the X_i are equally spaced; if a linear relation exists then one-half of the observations are selected at each end of the X-space; etc. Equally spaced values of X_i are often used in practice without regard to the form of the response function or to the most efficient selection of X_i values to estimate the parameters involved. Subsequently, a polynomial function is taken as the form for $f(\underline{\beta}, X_i, \epsilon_{ij})$ and orthogonal polynomials are used without regard to the true function of the Y_i, which may be exponential, say $Y_{ij} = \alpha X_i^{\beta} e^{\gamma X_i} + \epsilon_{ij}$ rather than of the polynomial form $Y_{ij} = \alpha + \sum_{g=1}^{p} \beta_g X_i^g + \epsilon_{ij}$. In any event the selection of levels of a factor or variable requires considerable thought on the part of the experimenter.

The above setting is similar to that for regression but it should be pointed out that the values of X_i could be varieties, brands, specimens, etc., for which there is no known grouping. Each of these categories then may be considered as a single factor at several levels.

2.3. Two or more factors each at several levels.

If two or more variables or factors each at two or more levels are in all possible combinations of the levels, the resulting treatment design is denoted as a factorial treatment design. Thus, any m-way, $m \geq 2$, classification in which no combination of the levels of the m-way classification is missing, fits the definition for a factorial (or complete factorial) treatment design. The individual combinations may occur an equal or an unequal number of times in the experiment. All that is required is that all possible treatment combinations are present at least once. Although this is the definition given by Yates [1937] in his Design and Analysis of Factorial Experiments, many writers appear to imply that the combinations must be replicated equally frequent in order for the treatment design to be a factorial. They consider the unequal numbers situation as a separate

topic, variously denoted as disproportionate numbers, unbalanced data, or messy data, if they consider it at all. Also, note that nothing in the definition restricts the distance between levels, i.e., equally spaced intervals are allowed but not required.

If some of the possible combinations in a complete factorial treatment design are missing or are deleted, a fractional replicate of a factorial treatment design or a partial factorial treatment design results. Whenever this occurs not as many treatment parameters can be estimated as when the complete factorial is present. This means that these parameters, if non-zero, will be partially or completely mixed up or confounded with the remaining treatment parameters. Thus, if we denote the single-degree-of-freedom treatment comparisons vector for the complete factorial as $\underline{\beta}$, an Nx1 column vector, and the Nx1 observation vector of treatment means as $\underline{Y}$, the expected value of the observations may be related to the parameters as follows:

$$E(\underline{Y}) = X\underline{\beta}$$

where X is the NxN design matrix or coefficient matrix relating the parameters and observations. Omitting the E part and partitioning, we may write

$$X\underline{\beta} = \begin{pmatrix} X_{11} & X_{12} \\ X_{21} & X_{22} \end{pmatrix} \begin{pmatrix} \underline{\beta}_1 \\ \underline{\beta}_2 \end{pmatrix} = \begin{pmatrix} \underline{Y}_1 \\ \underline{Y}_2 \end{pmatrix} = \underline{Y}$$

where X_{11} is pxp, X_{12} is px(N-p), X_{21} is (N-p)xp, X_{22} is (N-p)x(N-p), $\underline{\beta}_1$ and $\underline{Y}_1$ are px1, and $\underline{\beta}_2$ and $\underline{Y}_2$ are (N-p)x1. Now if $\underline{Y}_2$ observations, or combinations, are missing, or are omitted from the complete factorial, the remaining observations are:

$$\begin{pmatrix} X_{11} & X_{12} \end{pmatrix} \begin{pmatrix} \underset{\sim}{\beta}_1 \\ \underset{\sim}{\beta}_2 \end{pmatrix} = \underset{\sim}{Y}_1$$

or

$$X_{11}\underset{\sim}{\beta}_1 + X_{12}\underset{\sim}{\beta}_2 = \underset{\sim}{Y}_1 .$$

The normal equations for this situation are:

$$X_{11}'X_{11}\underset{\sim}{\beta}_1 + X_{11}'X_{12}\underset{\sim}{\beta}_2 = X_{11}'\underset{\sim}{Y}_1 .$$

If $X_{11}'X_{11}$ has an inverse (If not, one uses a generalized inverse and determines which parameters in $\underset{\sim}{\beta}_1$ can be estimated.), then $\underset{\sim}{\beta}_1 + \left(X_{11}'X_{11}\right)^{-1}X_{11}'X_{12}\underset{\sim}{\beta}_2$ $= \left(X_{11}'X_{11}\right)^{-1}X_{11}'\underset{\sim}{Y}_1$, and the parameters in $\underset{\sim}{\beta}_1$ <u>plus</u> a linear combination of some or all of the parameters in $\underset{\sim}{\beta}_2$ can be estimated. <u>Only if</u> the parameters in $\underset{\sim}{\beta}_2$ are truly zero (i.e., not assumed) can one obtain an estimate of the parameters in $\underset{\sim}{\beta}_1$.

If the quantity one can estimate in a 2^3 factorial experiment is A + AB + AC and if A is in $\underset{\sim}{\beta}_1$, and if AB and AC are in $\underset{\sim}{\beta}_2$ and not confounded with any other effect in $\underset{\sim}{\beta}_1$, then AB and AC are said to be <u>complete aliases</u> of A in that when one estimates A, one also estimates AB and AC, and vice versa. If, on the other hand, $A + \frac{1}{2}AB - \frac{1}{4}AC + \frac{1}{2}BC$ and $B + \frac{1}{4}AC - \frac{1}{2}AB + \frac{1}{2}BC$ are quantities that can be estimated, AB, AC, and BC are said to be <u>partial</u> or <u>fractional aliases</u> of A and B. The quantity $\left(X_{11}'X_{11}\right)^{-1}X_{11}'X_{12}$ is the <u>aliasing structure matrix</u>, and it defines the relationship between the parameters in $\underset{\sim}{\beta}_1$ and $\underset{\sim}{\beta}_2$.

The parameters of a factorial treatment design are designated as main effects of the factors and as interactions among the various factors. A <u>main effect</u> for a given factor say X_1 = A at a levels is designated as the set of a-1 single

degree of freedom contrasts among the a means, say $\bar{y}_{i\ldots}$ which are means of means over all levels of all other factors. An interaction between two factors (or a two-factor interaction) is the failure for the expected value of the differences between two levels of one factor to remain constant over all levels of the second factor, i.e., if $\bar{y}_{ij\ldots}$ is the mean of means over all other combinations then if $E\left(\bar{y}_{ij\cdot\cdot} - \bar{y}_{ij'\cdot\cdot}\,,\ j \neq j'\right)$ does not remain constant over all i, then a two-factor interaction is present. If the expected value of two factor interactions for a given value k of the third factor, $E\left(\bar{y}_{ijk\cdot\cdot} - \bar{y}_{ij'k\cdot\cdot} - \left(\bar{y}_{i'jk\cdot\cdot} - \bar{y}_{i'j'k\cdot\cdot}\right)\right)$, does not stay constant over all levels, k = 1,2,...,c, of the third factor, then a three-factor interaction is present. This form of the definition can be continued for any n-factor interaction in that if the differences in the levels between two (k-1)-factor interactions does not remain constant over all levels of the k-th factor then a k-factor interaction is present. In this sense, a main effect is a one-factor interaction.

In the usual textbook treatment of multiple regression, $E(\underset{\sim}{Y}) = X\underset{\sim}{\beta}_1$, $\underset{\sim}{B}_1$ is a kX1 vector of parameters given that k X-variables are available. This means that all interactions among the X-variables are not included in the parameter vector. Also, since it is possible to have a k-variable factorial for all X_i in the regression situation, multiple regression is a fractional replicate of a complete factorial treatment design. In this setting, a more realistic selection of the values of the X-variates and a more realistic interpretation of the results of a multiple regression experiment are possible.

2.4. Genetic designs.

A genetic treatment design is one which involves a set of parents and/or the derived progeny, where the progeny may be obtained by crossing, by asexual propagation, by use of mutagenic agents, by chromosomal manipulations, by ploidy,

or by other means. Genetic designs are constructed to elicit information on certain specified genetic phenomena. Animal and plant breeding investigations are concerned with the application of genetic principles, and hence a "plant breeding treatment design" would be included under the category of genetic design. It should be pointed out that many, if not all, genetic treatment designs may be included under one of the other five types listed herein. The first design discussed below may be an exception.

A common genetic design involves several generations of crossing of two parents and of the resulting crosses from the previous generations. For example, starting with two parents P_1 and P_2, only crosses of the form $P_1 \times P_2$, or its reciprocal $P_2 \times P_1$ can be made. This cross is denoted as the F_1 and is obtained as the first generation cross. The second generation of crosses using P_1, P_2, and F_1 as parents would be:

	females				Progeny		
males	P_1	P_2	F_1				
P_1	$P_1 \times P_1$	$P_1 \times P_2$	$P_1 \times F_1 = B_1$		P_1	F_1	B_1
P_2	$P_2 \times P_1 = F_1(R)$	$P_2 \times P_2$	$P_2 \times F_1 = B_2$	to produce	$F_1(R)$	P_2	B_2
F_1	$F_1 \times P_1 = B_1(R)$	$F_1 \times P_2 = B_2(R)$	$F_1 \times F_1 = F_2$		$B_1(R)$	$B_2(R)$	F_2

Thus, progenies available at the end of zero, one, and two generations are:

Generation	Progenies available
0	P_1, P_2
1	P_1, P_2, F_1, $F_1(R)$
2	P_1, P_2, F_1, $F_1(R)$, B_1, $B_1(R)$, B_2, $B_2(R)$

where the (R) means reciprocal cross; thus the reciprocal cross of the F_1 is denoted as $F_1(R)$.

At one stage, the above crossing plan resembles a two-factor factorial. If the reciprocal crosses $\left(F_1(R),\ B_1(R),\ \text{and}\ B_2(R)\right)$ are not included, a fractional replicate of a factorial results. Omitting the reciprocal crosses the following crosses are available in the third generation of crossing:

	females					
males	P_1	P_2	F_1	F_2	B_1	B_2
P_1	$P_1 \times P_1$	$P_1 \times P_2$	$P_1 \times F_1 = B_1$	$P_1 \times F_2$	$P_1 \times B_1$	$P_1 \times B_2$
P_2		$P_2 \times P_2$	$P_2 \times F_1 = B_2$	$P_2 \times F_2$	$P_2 \times B_1$	$P_2 \times B_2$
F_1			$F_1 \times F_1 = F_2$	$F_1 \times F_2$	$F_1 \times B_1$	$F_1 \times B_2$
F_2				$F_2 \times F_2 = F_3$	$F_2 \times B_1$	$F_2 \times B_2$
B_1					$B_1 \times B_1$	$B_1 \times B_2$
B_2						$B_2 \times B_2$

This plan may be continued for any number of generations, and there will be $k(k+1)/2$ crosses available in the $(n+1)$-st generation given that there were k crosses available in the nth generation.

All the entries above the diagonal are denoted as crosses, those on the diagonals, are denoted as selfs or selfed generations, and those below the diagonal in the above tables are denoted as reciprocal crosses. When the k entities to be crossed are different strains, the $k(k-1)/2$ crosses above the diagonal are denoted as a complete diallel crossing plan (CDC-plan). If only a partial set of these crosses are made, the resulting plan is termed a fractional or partial diallel crossing plan (PDC-plan). Thus, there are several possible diallel plans, as for example:

(i) all possible k(k-1)/2 crosses = CDC plan

(ii) " " " " plus the selfs (those on the diagonal) resulting in k(k+1)/2 combinations

(iii) all possible crosses, all selfs, and all possible reciprocal crosses resulting in k^2 combinations

(iv) all possible crosses and reciprocals resulting in k(k-1) combinations

(v) a fraction of the k^2 combinations not of the above forms (i) to (iv).

These plans have many uses outside the field of genetics. Some of these have been described by Federer [1967].

Another form of a diallel crossing plan is to use a set of k tester parents in all possible crosses with s different strains or lines. This plan would be of the form:

Tester parents

Strains	1	2	3	. . .	k
1	X	X	X	. . .	X
2	X	X	X	. . .	X
3	X	X	X	. . .	X
⋮	⋮				⋮
s	X	X	X	. . .	X

where X denotes a cross has been made. This would be the complete plan and a subset of these would produce a fractional or partial diallel crossing plan.

Not all genetic treatment designs can be put in the form of a partial or complete factorial treatment design. Some examples of genetic treatment designs of the nonfactorial structure would be those involving mutations, chromosomal additions or deletions, inversions of parts of chromosomes, translocations, ploidy, etc. Each one of these could be related to a one factor experiment but because of

the special nature of producing these genetic variants and because adequate controls must be included in genetic and breeding experiments, it was not considered to be appropriate to include them under one factor designs.

2.5. Nested or hierarchical designs

A nested or hierarchical design is one in which there are two or more factors each at two or more levels but for which there is no correspondence among the levels of the various factors or hierarchies; also, there may be subdivisions within each factor in a nested manner. If all the combinations of the factors were possible, a factorial treatment design would result. The nested or hierarchical treatment design may have several layers of nesting but there is no correspondence between levels of the various layers. If there were, a crossed (factorial) classification would result. An example of a hierarchical treatment design with two stages of nesting would be a designed experiment consisting of plant species, strains with species, and plants within species. Another example would be schools, teachers within schools, and students within teachers. A third two-stage nested example would be brands of skiis, types of skiis within brands, and individual pairs of skiis within types. Still other examples could be constructed but the nature of nested designs should now be apparent. In the examples given, there is no way of relating items within the first nesting with each other. For example, suppose that the teachers in school S_1 are numbered $1,2,\ldots,t_1$ and those in school S_2 are numbered $1,2,\ldots,t_2$. There is no more correspondence between number 1 in S_1 and number 1 in S_2 than there is between number 1 in S_1 and number 2 in S_2. There can be no correspondence unless there is a cross-classification which associates or relates the teachers in the two schools. Hence, the nested treatment design does not fit Yates' [1937] definition of a factorial or a fractional replicate of a factorial.

Several factors or categories not of the multiple regression type when all factorial combinations are possible, could be included under the nested type of treatment design.

2.6. Bioassay designs

A bioassay or a biological assay design refers to the selection of treatments used in an experiment for identifying the constitution or for estimating the potency of materials by their reaction on living material. Two analytical assay treatment designs are the slope ratio assay and the parallel line assay. The former assumes the response of the standard preparation to be $\hat{Y} = a + bX$ and of the test(unknown) preparation to be $\hat{Y} = a + bRX$, where X is the level of the preparation, and it is desired to estimate R. One can pick k levels of each preparation and the only known level of correspondence is the zero level of both preparations. There is no known correspondence between other levels of the two preparations. Hence, this type of treatment design cannot be classified as a factorial treatment design.

For the parallel line assay the response of the standard preparation is $\hat{Y} = a + b \log X$ and of the test (unknown) preparations $\hat{Y} = a + b \log R + b \log X$. This case resembles the nested treatment design in that there is no correspondence between the levels of the two preparations but it is desired to estimate the levels which do correspond for the two preparations and, hence, obtain a pseudo-factorial or an estimated factorial arrangement. If one takes anti-logs then $e^{Y} = aX^{b}$ for the standard preparation and $e^{Y}aR^{b}X^{b}$ for the test preparation; these coincide when R = 1 or when X equals zero in the same manner as for the slope ratio assay situation.

There are other bioassay treatment designs but the above should be sufficient to indicate the uniqueness of this type of design and the need for a separate category or type.

3. PROPERTIES OF TREATMENT DESIGNS

3.1. Balance

3.1.1. Yates' definition of balanced confounding or "order-balance." Yates [1937] defined the term balanced confounding to be an incomplete block design for which all effects of a specified order, say, all two factor interactions, are confounded with incomplete block differences an equal number of times. Although Yates [1937] does not formally state this definition, it is implied. An implication from the above statement of the definition is that it holds for s^m as well as for $s_1 s_2 \cdots s_m = \prod_{i=1}^{m} s_i$ factorials where there are m factors, $A_1, A_2, \ldots, A_m$, with $s_1, s_2, \ldots, s_m$ levels, respectively; in the s^m factorial the s_i are all equal to s levels for each factor. This, however, would imply that unequal block sizes would be utilized for unequal s_i whereas equi-size blocks would be utilized when $s_i = s$.

This definition assures that all effects of a given order for s^m factorials will be estimated with the same variance (assuming homoscedasticity). In order to extend this concept to the $\prod_{i=1}^{m} s_i$ factorial, perhaps it would be sufficient to say that every normalized contrast of effects of a given order be estimated with the same variance (assuming homoscedasticity within blocks of unequal sizes).

3.1.2. Pairwise balance

If every effect is confounded an equal number of times with incomplete block differences, the design is said to be pairwise balanced. This definition corresponds to the ordinary pairwise balance definition for a balanced incomplete block experiment design wherein every possible pair of combinations occurs together equally frequently in the blocks [see e.g., BU-394-M]. Although this has been ascertained for s^m factorials, it is not certain that it holds equally well for $\prod_{i=1}^{m} s_i$ factorials with unequal block sizes which are functions of the s_i. When the s_i are all equal to s, then the design would also be variance-balanced in the same sense as for experiment designs. However, with unequal s_i it would appear that the variances would be unequal.

3.2. Properties of fractionally replicated plans.

3.2.1. Regular and irregular fractions. A regular fractional replicate is defined to be one in which only complete alias of the parameters in $\underline{\beta}_1$ with those in $\underline{\beta}_2$ exist (see section 2.3); if any degree of partial aliasing exists, the fraction is said to be irregular. Another, and perhaps equivalent, definition given by Raktoe and Federer [1965] is a geometric one. Since it is known that an (m-n)-flat, $n \leq m$, of EG(m,s) consists of s^{m-n} points, they define a fraction $\underline{Y}_1$ to be regular if it is a s^{-n} fraction of s^m and if the corresponding subset forms an (m-n)-flat of EG(m,s) and to be irregular otherwise. Or, more simply, the fraction $\underline{Y}_1$ is regular if it is observed at an (m-n)-flat of EG(m,s).

3.2.2. Balanced resolution V fractional replicates of the 2^m factorial. Srivastava and Chopra [1971] define a resolution V fractional replicate of the 2^m (a plan which allows estimation of all main effect and all two-factor interactions) as follows: Let $\hat{A}_i$ represent the estimate of the main effect parameter for the ith factor, $i = 1,2,\ldots,m$, $\hat{\mu}$ = the estimate of the general mean, and $\hat{A}_{ij}$ = the estimate of the two-factor interaction effect between factors A_i and A_j. Then, if V(D) is the variance-covariance matrix of the estimated parameters and if the design or plan D has the property of being balanced, V(D) must be such that $\mathrm{Var}(\hat{A}_i)$, $\mathrm{Var}(\hat{A}_{ij})$, $\mathrm{Cov}(\hat{\mu},\hat{A}_i)$, $\mathrm{Cov}(\hat{\mu},\hat{A}_{ij})$, $\mathrm{Cov}(\hat{A}_i,\hat{A}_j)$, $\mathrm{Cov}(\hat{A}_i,\hat{A}_{ij})$, $\mathrm{Cov}(\hat{A}_i,\hat{A}_{jk})$, $\mathrm{Cov}(\hat{A}_{ij},\hat{A}_{jk})$, and $\mathrm{Cov}(\hat{A}_{ij},\hat{A}_{kl})$ are independent of $i,j,k,l = 1,2,3,\ldots,m$. They note that this definition of a balanced resolution V fractional replicate of a 2^m factorial is equivalent to requiring that the plan D be a balanced array of strength 4 (see Chakravarti [1956]).

3.2.3. Rotatability. A fractional replicate of a factorial possesses the property of rotatability if upon replication of the center point of the plan n_1 times, n_1 is such that every contrast has the same variance on a circle r units from the

center point of the region, i.e., for all points for which $X_{1u}^2 + X_{2u}^2 + \cdots + X_{mn}^2 = \rho^2$ = a constant given that X_{iu}, i = 1,2,...,m, represent the coordinates of a point (see Box and Hunter [1957]). For exploratory work on response surfaces when the experimenter does not know in advance how the response surface will be oriented, this is a useful criterion to use.

3.2.4. An invariance property of a fractional replicate. Suppose that D is an $(m(s-1) + 1) \times m(s-1)$ fractional replicate plan of an s^m factorial for estimating the mean and main effect parameters in $\underset{\sim}{\beta}_1$; the elements in any column run from 0,1,...,s-1. Let X_{11} be the treatment contrast matrix corresponding the parameters in $\underset{\sim}{\beta}_1$ with the observations for the combinations in the plan D. Then, if any treatment combination, say, $i_1, i_2, \ldots, i_m$ for $i_j = 0,1,2,\ldots,s-1$, j = 1,2,...,m is added to every treatment combination in plan D, modulo s, and if $X_{11,v}$ is the treatment contrast matrix corresponding to this new plan, then Paik and Federer [1970a] have shown that $||X_{11}'X_{11}|| = ||X_{11,v}'X_{11,v}||$. This means that the determinant of the matrix $X_{11}'X_{11}$ remains invariant under the above addition procedure. This follows from the fact that the addition procedure merely changes the labelling of the levels of a factor and hence the total information remains the same for any given factor. For the 2^m factorial this addition procedure holds for any saturated plan and not only the saturated main effect plan; in the 2^m factorial, a relabelling of the levels does not change the interaction, except possibly for sign. Hence, $||X_{11}'X_{11}||$, which is p×p, will remain invariant under this procedure as was shown by Paik and Federer [1970c].

Srivastava, Raktoe and Pesotan [1971] extended the addition procedure to cover saturated main effect plans for the $\prod_{i=1}^{m} s_i$ factorial. Here again, a relabelling of the levels of any given factor does not change the total information on any given main effect.

3.2.5. Semi-invariance property of the aliasing structure matrix. The aliasing structure matrix, $\left(X_{11}'X_{11}\right)^{-1}X_{11}'X_{12}$, is said to be semi-invariant if the coefficients remain the same except for sign. Thus, if a plan D undergoes the addition procedure described in section 3.2.4., then the aliasing structure matrix for saturated fractional replicates from a 2^m factorial remains semi-invariant under the addition procedure (see Paik and Federer [1970c]). This follows because a relabelling of the levels of two or more factors will only affect the sign of the resulting interactions in the 2^m factorial.

3.2.6. Aliasing structure property. Paik and Federer [1970b] have partially defined a property of the aliasing structure matrix $\left(X_{11}'X_{11}\right)^{-1}X_{11}'X_{12} = A$, say. If there are only complete aliases of the parameters in $\underset{\sim}{\beta}_1$ and $\underset{\sim}{\beta}_2$ this is defined to be the best situation since the number of effects that are to be estimated as a sum of effects is minimal. The worst situation is when all effects in $\underset{\sim}{\beta}_2$ are partial aliases of any one effect in $\underset{\sim}{\beta}_1$. A characterization of all such aliasing structure matrices is needed; one characterization could be to count the number of zeros as the more zeros present, the fewer the number of partial aliases.

The number and nature of effects which are completely or partially confounded could be more important to the experimenter than any of the other criteria that might be used. Since this is a potentially useful criterion, a study of this property is desirable.

3.2.7. Variance optimality. In certain situations, the experimenter might wish to have a plan which results in minimum variances for the estimated effects for $\underset{\sim}{\beta}_1$. In this case he might wish to have the trace of $\left(X_{11}'X_{11}\right)^{-1}$ a minimum. In other cases, the experimenter might wish to select a plan which minimizes the determinant of $\left(X_{11}'X_{11}\right)^{-1}$. Paik and Federer [1970b] have obtained saturated main effect plans for the 2^2, 2^3, 2^4, 3^2, and 3^3 which achieve these properties; they

have characterized all saturated main effect plans for 2^2, 2^3, and 2^4 by the value of the determinant of $X_{11}'X_{11}$. The generators of all possible plans under the addition procedure described above have been enumerated for the 2^2, 2^3, and 2^4 factorials.

4. PROCEDURES

Procedure for selecting treatments to be used in experiments should not be confused with properties of treatment designs. For this reason, some of the procedures are mentioned in a separate section.

4.1. One- and multi-stage.

There are many procedures for conducting an experiment. If all the v treatments being compared are included in one experiment at one time then this is called a one-stage procedure. If sets of v treatments are applied to a set of rv experimental units successively or simultaneously, this is termed a multi-stage procedure.

4.2 Sequential.

If, in a multi-stage experiment, the results for treatments at the ith stage determine which treatments are to be included in the i+1st stage, then this is denoted as a sequential procedure. For example, in a $\prod_{i=1}^{m} s_i$ factorial the experimenter may select t_1 treatment combinations to experiment with at stage one; then, based on the results from these t_1 combinations, he selects t_2 combinations for stage 2; etc. The experimenter may or may not include repetition of a single combination before completing all treatment combinations.

The selection of the new set of treatments for the i+1st stage may be made to obtain a desired property in connection with the results for the previous treatments. For example, if a minimum value of the determinant of $\left(X_{11}'X_{11}\right)^{-1}$ is required at each stage, then the additional combinations will be such that the

desired new parameters from β_2 will be estimated and the determinant of the variance-covariance matrix for all estimated parameters at stages 1 and 2 will be a minimum.

4.3. Augmentation.

A given treatment design may be selected, e.g., a complete factorial of m factors, and it may be decided to augment this treatment design with controls or with combinations outside the range of levels or factors in the complete factorial. The procedure of augmenting a treatment design would be to attain some specific property or goal not best achieved by a given treatment design.

Although augmentation is described as a procedure here it could also be described as a principle as it was for experiment design in BU-394-M.

5. SOME UNSOLVED PROBLEMS

The unsolved problems are so varied and numerous that specific problems will not be discussed here. Instead, some general problems will be mentioned. Perhaps the first problem is to rethink and to rewrite the present report and to include omitted results. With regard to any definition or property, it is necessary to characterize that item, to find alternative definitions and properties, to show equivalences and non-equivalences between the alternative expressions, to consider economic alternatives, and to consider several alternatives simultaneously. A detailed and thorough study of each of the properties described in section 3 would prove fruitful. There are studies of various kinds now being conducted but a more general approach may lead to the desired advances in this area.

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