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Abstract

2^k full factorial designs may be prohibitively expensive when the number of factors k is large. The most popular technique developed to reduce the number of treatment combinations is the fractional factorial design; confounding in estimating the model parameters naturally results in various resolution and aberration levels. While very useful, these resolution levels may not satisfy experimenters' requirements for estimability and cost reduction. For example, while Resolution V ensures a common requirement that no two-factor interactions are confounded, it also imposes an often undesired restriction that a main effect cannot be confounded with a three-factor interaction, which may very well be non-existent or negligible. We propose a new concept of "active confounding avoidance" whose goal is to identify, for given any set of parameters, a set of treatment combinations such that estimates of the parameters are not confounded with one another. We show that the "least-treatment-combinations" methods developed for identifying a minimal set of m treatment combinations for a 2^k model with only m non-zero parameters achieve this goal. We then propose a simple design pattern that achieves active confounding avoidance for parameters spanning from all main effects up to all i -factor interactions, for all $i = 1, 2, \dots, k$, all with the least number of treatment combinations. The pattern also specifies how treatment combinations should be sequenced for experimentation according to a parameter sequence of decreasing magnitude possibly specified by the experimenter based on prior knowledge. The former sequence is optimal in that the experimentation can stop whenever the current model is deemed adequate and experiments already conducted could be considered necessary.

Keywords: Design of experiment, Two-level factorial design, Sequential design, Resolution, Optimal design, Run minimization

1. Introduction

A full 2^k factorial design may be prohibitively expensive when the number of factors k is large. In the semiconductor-fabrication industry, one complete experimental run of a new “recipe” for wafer fabrication may cost \$20,000 and may take one month. Minimizing the number of treatment combinations yet ensuring statistical validity is a critical task. In that and some other mature industries, much domain knowledge and past experience has accumulated regarding presence or absence of interactions among some of the experimental factors. However, the exact magnitudes of some existent interactions must still be estimated through experimentation.

Techniques have been developed to reduce the number of treatment combinations from 2^k to smaller numbers. The approach of fractional factorial designs 2^{k-p} is the most popular of all; confounding in estimating the model parameters naturally results (Box et al., 1978; Montgomery, 2009). The main goal is to reduce the number of treatment combinations by 2^p fold to only 2^{k-p} treatment combinations, $1 \leq p < k$. The resolution level, e.g., III, IV and V, is an indicator of confounding degree for any such design, often supplemented with the aberration level. Closely related techniques include saturated (resolution III) designs, resolution IV designs, resolution V designs, supersaturated designs. Other techniques include Plackett-Burman designs (Montgomery, 2009), Taguchi orthogonal-array designs (Taguchi and Konishi, 1987), etc.

Strengths of fractional factorial designs include ease of generation (i.e., specification) of the required treatment combinations and ease of arithmetic computation needed for estimation. In

addition, the generators of the required treatment combinations can be used to easily identify all alias sets, where each set of aliases specifies a group of effects/interactions whose sum or another simple linear combination is estimable but none of which is estimable alone. Multiple 2^{k-p} designs exist for any k and p pair. The effects/interactions of an alias set are said to be confounded, and if and only if exactly one particular effect/interaction of an alias set is non-zero, such confounding poses no estimation difficulty. In general, such difficulty may exist; the experimenter needs to select one from the multiple and often many 2^{k-p} designs that has the highest level of resolution (and perhaps also lowest level of aberration) (Montgomery, 2009), where, for example, confounding of a main effect only with two-factor or higher-order interactions is considered as having a higher resolution than confounding among some of the main effects themselves. We consider this kind of resolution maximization as a secondary objective, subjected to the primary concern of the alias-based fraction-generation method, and as passive resolution selection, from among the choices provided by the fraction-generation method. We propose in this paper a new concept of active confounding avoidance. Given any set of parameters, its goal is to identify a set of treatment combinations so that, their estimates are not confounded with one another. For example, a common desire of an experimenter, and hence a common requirement for a designed experiment, is to estimate all main effects and all two-factor interactions without confounding among them. While resolution IV cannot achieve this, resolution V is more than necessary, because it also imposes an often undesired restriction that a main effect cannot be confounded with a three-factor interaction, which may very well not exist or may be considered negligible. For ease of discussion, we refer to all designs enabling main effects and all interactions involving i or fewer factors to be estimated without confounding among themselves as a 2^{k_i} (reduced) design. Those designs satisfying the common desire and

requirement just mentioned are the special case $2^{k,2}$. A saturated design is the special case of $2^{k,1}$; a full factorial is the special case of $2^{k,k}$. We propose in this paper a simple design pattern that achieves active confounding avoidance for $2^{k,i}$ for all $i = 1, 2, \dots, k$. Also for ease of discussion, we refer to the regression model obtained by removing from the 2^k full regression model all interactions involving $i+1$ or more factors as a $2^{k,i}$ (reduced) model. We will also refer to the $2^{k,i}$ (reduced) model or design as the i -th degree (reduced) model or design.

Motivated by the issue of prohibitive cost of 2^k designs when k is large, Tsao and Wibowo (2005) pointed out that when only m of the 2^k effects/interactions may be non-zero, only m treatment combinations are required for their estimation. With their estimation, one can build an adequate regression model. In that work as well as in this paper, a regression model is considered adequate if (a) each of the 2^k mean responses can be expressed as a function of statistically significant (i.e., the non-zero) effects/interactions plus a random observation error term that is independent of other error terms and (b) the significant effects/interactions can be estimated without confounding among themselves. They developed a method, based on the Phase-I Simplex Method for linear programming, to identify a minimal set of exactly m treatment combinations to estimate the m non-zero effects/interactions. Performing experiments for these m treatment combinations, typically with replications, allows estimation of the m corresponding mean responses. The m non-zero effects/interactions can be estimated by solving the m equations defining the m mean responses as m functions of the 2^k effects/interactions, but with the $2^k - m$ zero effects/interactions substituted by 0. We refer to that method as a least-treatment-combinations method or simply least-combinations method. That method and the

methods to be proposed in this paper deal with estimability of parameters, i.e., unbiased estimation of parameters, but not estimation accuracy. Analysis of estimation accuracy requires knowledge of the sample size for each treatment combination, and methods developed to minimize the total amount of experimental effort may be called least-runs methods. We show in this paper that any of the m effects/interactions estimated with the m treatment combinations produced by the least-treatment-combinations method of Tsao and Wibowo (2005) is not confounded with any other. This is also true for an improved least-treatment-combinations method proposed in Tsao and Liu (2008).

Both of these two previous studies proposed “numerical algorithms” to search for qualified minimal sets of treatment combinations. The simple pattern to be proposed in this paper is in an explicit and intuitive form and can be truncated to produce least-treatment-combinations $2^{k,i}$ (reduced) designs which produce estimates for the main effects and all interactions involving i or fewer factors, all without confounding among them.

Often in practical applications of the fractional factorial designs, a 2^{k-p} fractional design is deemed as inadequate, and a 2^{k-p+1} design becomes necessary. Adding another 2^{k-p} fractional design in general and fold-over in specific are common strategies. Either way, the treatment combinations of the former smaller design are part of those of the latter larger design, so as to reuse all the results of all the experiments already conducted. We refer to this phenomenon “forward compatibility.” This compatibility is critical in practice, particularly when experiments are expensive and time consuming. We propose a method to expand a $2^{k,i}$ design to a $2^{k,i+1}$ design so that all the treatment combinations of the $2^{k,i}$ are part of those of the $2^{k,i+1}$ design.

The number of treatment combinations of a $2^{k,i+1}$ design may be much larger than that of a $2^{k,i}$ design. While some $(i+1)$ -factor interactions may be non-zero, some others may actually be zero or negligible. Therefore, opportunities exist to identify treatment combinations of $2^{k,i+1}$ for elimination, in order to reduce the number of treatment combinations while maintaining the estimability of the non-zero $(i+1)$ -factor interactions. The experimenter may know, based on the domain knowledge or prior data analysis, or may be willing to assume that a strong interaction does exist between a particular set of $(i+1)$ factors while a weak or no interaction exists between another particular set (e.g., Zhang and Huang, 2010). In such a case, the experimenter may regard the former interaction as more important than the latter. With such knowledge or assumptions, the experimenter may be able to sequence all interactions among any $i+1$ factors, e.g., all two-factor interactions, in a non-increasing order of importance or magnitude. (This sequencing does not have to be done for individual effects/interactions and can be performed for blocks of them, where a block represents a set of effects/interactions of indistinguishable magnitudes.)

In photolithography of semiconductor manufacturing, main factors influencing the extent of etching include acid concentration, temperature, moisture level, duration, etc. Although the exact factor effects or interactions associated with the photolithography step of a new processing recipe are unknown and must be determined through experimentation, domain knowledge accumulated through prior experience, including screening and optimization experiments and production runs, can inform the process engineer about the relative importance of these factors, in their nominal operational ranges, and even about the relative importance of some of their

interactions. For example, at the level of factor effect in a 2^k experiment, acid concentration is considered in general to be more important than the temperature, which is in turn considered as more important than the moisture level. At the interaction level, the interaction between temperature and acid concentration is considered in general as more important than the interaction between temperature and moisture level.

The method we propose actually expands a $2^{k,i}$ design to a $2^{k,i+1}$ design sequentially, with one more treatment combination at a time for estimating one more $(i+1)$ -factor interaction. If the experimenter can sequence the magnitudes of all the $(i+1)$ -factor interactions in a non-increasing order, the proposed method achieves the expansion with a corresponding sequence of treatment combinations, with forward compatibility and active confounding avoidance. To the experimenter, this sequence is optimal in that the experimentation can stop whenever the current model is deemed adequate and experiments already conducted could be considered necessary.

This paper is organized as follows. Section 2 focuses on the 2^4 factorial design and use it to illustrate the main contributions of this paper, including the concepts of active confounding avoidance, least-treatment-combinations design and $2^{k,i}$ (reduced) design, the main objectives, the solution algorithms, and their applications. Section 3 defines the problem in the general context of full 2^k factorial design. Section 4 shows that the least-treatment-combinations methods of Tsao and Wibowo (2005) and Tsao and Liu (2008) achieve active confounding avoidance. Section 5 develops an algorithm for identifying a $2^{k,i}$ design for estimating all the effects/interactions of a $2^{k,i}$ model with forward compatibility, active confounding avoidance and least treatment combinations. It also develops an algorithm that expands incrementally a $2^{k,i}$

design to a $2^{k,i+1}$ design, with one additional treatment combination at a time for estimating the next most important $(i+1)$ -factor interaction. The two algorithms starts with an initial treatment combination and construct the designs, and the initial treatment combination is the one with each factor set at its low (-) level. Some applications of the proposed methods and their comparisons with prevailing methods are provided in Section 6. Concluding remarks are given in Section 7.

2. Background, Problem Description and Main Results, via the 2^4 Factorial Design

We use the 2^4 factorial design to motivate the problems being investigated and to illustrate the solutions and their applications. We focus on the intuitive design pattern and use it to illustrate the other main contributions, including least treatment combinations, active confounding avoidance, and forward compatibility.

We first describe the full 2^4 factorial design and then discuss reduced designs $2^{4,0}$, $2^{4,1}$, $2^{4,2}$ and $2^{4,3}$. ($2^{4,4}$ is actually the full 2^4 design.) The four factors are denoted as Factors A, B, C and D. Sixteen, i.e., 2^4 , treatment combinations are required in the full factorial design.

To define a full regression model for the design, we use the following conventional notation. G denotes the grand effect; A, B, C, and D denote the four main effects; AB, AC, AD, BC, BD and CD denote the six two-factor interactions; ABC, ABD, ACD and BCD denote the four three-factor interactions; ABCD denotes the four-factor interaction. In the notation just defined, the full regression model for the 2^4 factorial design is:

$$Y_{X_A X_B X_C X_D ; r} = \mu_{X_A X_B X_C X_D} + \varepsilon_{X_A X_B X_C X_D ; r} \quad (1)$$

$$\begin{aligned} \text{where } \mu_{X_A X_B X_C X_D} = & G + \frac{A}{2}x_A + \frac{B}{2}x_B + \frac{C}{2}x_C + \frac{D}{2}x_D \\ & + \frac{AB}{2}x_Ax_B + \frac{AC}{2}x_Ax_C + \frac{AD}{2}x_Ax_D + \frac{BC}{2}x_Bx_C + \frac{BD}{2}x_Bx_D + \frac{CD}{2}x_Cx_D \\ & + \frac{ABC}{2}x_Ax_Bx_C + \frac{ABD}{2}x_Ax_Bx_D + \frac{ACD}{2}x_Ax_Cx_D + \frac{BCD}{2}x_Bx_Cx_D + \frac{ABCD}{2}x_Ax_Bx_Cx_D, \end{aligned} \quad (2)$$

$x_i = \pm 1$ for $i=A, B, C$ and D , $r = 1, 2, \dots, n$, and n is the number of replications. As usual, we use A, B, C and D to denote the Factors A, B, C and D as well as the main effects of Factors A, B, C and D .

Estimating the 2^k mean responses of a 2^k experiment is only a stepping stone toward the estimation of the 2^k effects/interactions. This paper focuses mainly on the relationship between the 2^k mean responses and the 2^k effects/interactions and how the former can be used to determine the latter. Thus, Eq. (2), in this special case, plays a key role. With Eq. (2), all 16 effects/interactions can be solved explicitly as functions of the 16 mean responses once these 16 mean responses have been estimated. In fact, the solution is easy and can be virtually performed with an inspection of the design matrix, due to the orthogonality between any pair of columns of the matrix associated with the right-hand side of Eq. (2). Table 1 depicts Eq. (2) and facilitates the solution process with visual inspection. The order in which the treatment combinations appear as rows of the matrix adheres to the convention of “standard order.” For ease of reference, the treatment combinations and the corresponding mean responses are labeled 1 through 16 accordingly.

When only m of the 16 effects/interactions are non-zero, not all 16 treatment combinations are required for estimation of the non-zero ones. Tsao and Wibowo (2005) developed a least-treatment-combinations method, based on the phase-I simplex method, to identify a set of m treatment combinations that suffices for the estimation of the m unknown effects/interactions. Such a set of effects/interactions has been referred to in the literature as a “requirement set,” e.g., Franklin, 1985; Ke and Tang, 2003. These researchers and many others, e.g., Hedayat and Pesotan (1997), developed methods and algorithms to find good designs, according to various criteria, for estimating all the parameters of such a requirement set, particularly the set of all main effects and some of the two-factor interactions deemed important by the experimenter. Tsao and Liu (2008) developed a sequential least-treatment-combinations method to identify one additional treatment combination for each additional effect/interaction of a given sequence of effects/interactions of non-increasing order in magnitude. Such sequencing of factor effects/interactions for the purpose of minimizing the number of treatment combinations to experiment was first proposed in Tsao and Liu (2008); it was motivated by, among other reasons, the fact that the zero-non-zero dichotomy required of all the “requirement set” studies may not be completely clear to the experimenter, particularly during the exploratory stage of experimentation. In addition, experimenters often have some prior domain knowledge about the relative importance or magnitude of different factors or their interactions. Box et al. (1978), in their commentaries on the examples given in the chapter More Applications of Fractional Factorial Designs, recognized the necessity for experimenters to use judgment for efficiency, with a calculated risk. This sequencing of effects/interactions and the corresponding sequencing of treatment combinations proposed in Tsao and Liu (2008) and in this paper provides experimenters new ways to formulate judgment and improve efficiency.

These sequencing proposals have been intended for cost minimization without sacrificing statistical validity. Statistical tests that should be conducted to ensure such validity were addressed in Tsao and Liu (2008), including a thorough diagnostic check after experimenting for each additional treatment combination to estimate one more effect/interaction. As discussed in detail in Tsao and Liu (2008), the sequential experimentation can be implemented block by block, where a block represents a set of effects/interactions of indistinguishable magnitudes. In semiconductor manufacturing, various researchers, e.g., Shan et al. (2001), Braha and Shmilovici (2003) and Zhang and Huang (2010), have studied the interactions among multiple “functional process variables” (FPV’s) and developed dynamic models for the purpose of early detection of out-of-control process. Such models have been used to produce cardinal predictions of interactions in process control and to judge ordinal rankings of their importance or magnitude in design of experiments.

We use the design matrix of Table 2 for motivating the problem and the solution method and for illustrating uses of our method. Table 3 focuses on the treatment combinations produced by the proposed method and uses – and + to specify the treatment combinations for higher clarity. As will be made clear later, the sequence of those treatment combinations that are needed for $2^{4,i+1}$ design but have not been included in $2^{4,i}$ design may vary, depending on the order of decreasing (or non-increasing) magnitude of the new parameters of the $2^{4,i+1}$ model as possibly judged by the experimenter. This example assumes that the magnitude order coincides with the nominal “alphabetic” ordering of all the parameters, without loss of generality.

For each of the reduced designs $2^{4,0}$, $2^{4,1}$, $2^{4,2}$, $2^{4,3}$ and $2^{4,4} = 2^4$, we first illustrate the fact that the design suffices for estimating all the parameters of corresponding reduced models and then discuss the features of least treatment combinations, active confounding avoidance and forward compatibility. In discussing estimability for $2^{4,i}$, all interactions involving $i+1$ or a greater number of factors are assumed to be zero. When this assumption is relaxed, the issue of confounding becomes relevant; so is the feature of active confounding avoidance.

$2^{4,0}$ is the 0-th degree reduced design for the factorial model 2^4 . In the corresponding reduced model, only G of all the 2^4 parameters is considered as non-zero. Under this assumption, TC1 alone enables estimation of G. Now move on to $2^{4,1}$, the 1st-degree reduced design for the factorial model 2^4 . In the corresponding reduced model, only G, A, B, C, and D of all 2^4 parameters are considered as non-zero. The method to be proposed in the next sections produces four additional treatment combinations TC2, TC3, TC5 and TC9. They, together with TC1, suffice for estimating G, A, B, C and D for the following reasons. We first explain the estimability of A, B, C and D, and then that of G. First, compare TC1 and TC2. The only difference in treatment between TC1 and TC2 is the treatment for Factor A, with TC1 set at the low (-1) level of A and TC2 set at the high (+1) level of A and with all other factors set at the same low level (-1). Under the assumption that all interactions are zero in general and, in particular, no interaction exists between Factor A and any of the three other factors, A can be estimated. Similar reasoning establishes the further estimability of B, C and D. Given that A, B, C, and D have all been estimated, G can be estimated with any of the five TCs. Since there are five parameters and exactly five treatment combinations constitute the $2^{4,1}$ design, this design requires least treatment combinations. By the estimability of G, A, B, C, and D, the 5×5 matrix

delineated in Table 2 by columns G, A, B, C and D and rows TC1, TC2, TC3, TC5 and TC9 is invertible and has an inverse matrix. Pre-multiplying the first five rows of the full design matrix of Table 2 in its entirety by this inverse matrix produces a 5×5 identity matrix as the first five columns. Regardless what the other columns turn out to be, this 5×5 identity matrix ensures no confounding among the estimates of G, A, B, C and D. Finally, note that the reasoning so far does not depend on the order in which the main effects A, B, C and D are estimated. The order can be determined according to decreasing (or non-increasing) magnitude. This independence implies forward compatibility.

Now that the estimability of the five parameters G, A, B, C and D of $2^{4,1}$ has been established with TC1, TC2, TC3, TC5 and TC9, let us move on to estimating the parameters of $2^{4,2}$ all two-factor interactions as well as all main effects, under the assumption that all higher-order interactions are zero in general and, in particular, no interactions exist among any three factors of the four. Note that combining the new treatment combination of TC4 with three of the five treatment combinations already selected, namely TC1, TC2, and TC3, produces a *full factorial* for Factors A and B. This and the fact that the Factor C and Factor D of all four treatment combinations are set at the same low level of -1 ensure the estimability of interaction AB, given the assumption that no three-factor or four-factor interactions exist. The same reasoning can be used to establish the estimability of interaction AC. Note that once the estimability of all the parameters of $2^{4,1}$ has been established with TC1, TC2, TC3, TC5 and TC9, establishing the estimability of interaction AC and establishing that of interaction AB are completely independent. In particular, the estimability of AC does not depend on that of AB and vice versa. This is a key reason behind the forward compatibility for incremental inclusion of two-factor

interactions. For similar reasons, AD, BC, BD and CD can be estimated incrementally with inclusion of treatment combinations of TC10, TC7, TC11 and TC13, respectively. With all the two-factor interactions estimated, all main effects and the grand effect can be estimated; the reasoning is similar to the case of $2^{4,1}$. Therefore, this $2^{4,2}$ design consists of TC1; TC2, TC3, TC5, TC9; TC4, TC6, TC10, TC7, TC11, TC13. It is apparent that all the treatment combinations of $2^{4,1}$ design are part of those of $2^{4,2}$ design. This illustrates the forward compatibility from the $2^{4,1}$ design to the $2^{4,2}$ design. The features of least treatment combinations and active confounding avoidance should be clear.

With all main effects and two-factor interactions estimated with the results of treatment combinations just identified and with the assumption that the interaction among the four factors is zero, we can estimate the four three-factor interactions ABC, ABD, ACD and BCD with TC8, TC12, TC14 and TC15. The reasoning is similar to what was just put forward for estimating all two-factor interactions.

We provided intuitive reasoning so far. We now use the estimation process for ABC with TC8 (+++-), as summarized in Table 4, to illustrate the process and to motivate the proof for the general 2^k context. Focus on only the treatment combinations generating the full factorial for Factors A, B and C. In other words, ignore the rows shaded in grey. Since Factor D is set at the low level for all these focal treatment combinations and the interaction ABCD is considered as zero for building the current $2^{k,3}$ design, this full factorial can indeed be used to estimate all the effects/interactions of the full factorial for Factors A, B and C. Of particular interest is the estimate of ABC, which will not change when more treatment combinations are included for

estimating some or all of the other 3-factor interactions. (The estimates for A, B and C, however, will change when this happens.)

The estimator for ABC is simply the inner product of the ABC column and the mean response (m.r.) column but divided by the usual divisor 4 for this 3-factor factorial. Note that, at this stage, 12 treatment combinations have been selected, and the 12 relevant mean responses are $u_1; u_2, u_3, u_5, u_9; u_4, u_6, u_{10}, u_7, u_{11}, u_{13}; u_8$. Substituting the mean responses of the 8 non-shaded rows with the linear combinations of effects/interactions specified in those rows and simplifying the expression produces

$$f(u_1; u_2, u_3, u_5, u_9; u_4, u_6, u_{10}, u_7, u_{11}, u_{13}; u_8) = (-u_1 + u_2 + u_3 + u_5 - u_4 - u_6 - u_7 + u_8) / 4 = ABC$$

The reason is as follows. The 12 columns of the design matrix can be partitioned into two groups. Group 1 consists of those whose effects/interactions are parameters of the full factorial of Factors A, B and C. Group 2 consists of the others; they are marked in Table 4 with light grey. The (non-shaded portion of) column ABC is orthogonal to all the other columns of its group, because of their constituting a full factorial. Each of the four columns of group 2 is the result of one of the (non-ABC) column of the ABC full factorial multiplied by the constant -1, which is the low level set for Factor D for all the treatment combinations of the ABC full factorial. The orthogonality among the ABC full-factorial columns implies the orthogonality between the (non-shaded portion of) ABC column with its counterparts in group 2.

The reasoning for the use of one additional TC12 (++-+) to estimate ABD is similar. An important observation to recall is that estimating ABD will not change the estimate already obtained for ABC because the estimator of ABC does not involve the mean response of treatment combination TC12.

When (a) all the parameters of a $2^{4,i}$ model are estimated, (b) model adequacy checking reveals the need for inclusion of some $(i+1)$ -factor interactions, and (c) all the $(i+1)$ -factor interactions can be sequenced in a non-increasing order of their magnitudes, the treatment combination identified for estimating each of the $(i+1)$ -factor interaction can be sequenced accordingly so that experimentation can be stopped when an adequate regression model is built, before all of the treatment combinations identified for all the $(i+1)$ -factor interactions are experimented. It should be clear, for example, that if the sequence for all two-factor interactions is AC, AD, BC, BD, CD and AB (with AB being the smallest one and with the others ordered as in the default order), the corresponding treatment-combination sequence is TC6, TC10, TC7, TC11, TC13, and TC4 (with the treatment combinations re-sequenced exactly the same way).

3. Problem Definition

We now define the problem. To facilitate the discussion, we adopt a set of notation that is more amenable for addressing the general case of 2^k factorial design. It is the same set of notation used in Tsao and Liu (2008) and Tsao and Patel (2011) except that the index for the factors used in this paper is j , instead of i . (The index i is used in this paper to denote the maximum number of factors whose interactions are considered. In other words, it denotes the degree i of the reduced regression model, as in a $2^{k,i}$ model or a $2^{k,i}$ design.) Let j be the index for the factors, $j =$

1, 2, ..., k. Denote the grand effect as e_G . Denote the effect of factor j as $e_j, j = 1, 2, \dots, k$. Let $j_l, l = 1, \dots, k$, denote a factor 1, 2, ..., or k , and when L arbitrary factors appear in a subscript, the subscript is denoted as $j_1 j_2 \dots j_l \dots j_L$ and the factors appear in ascending order of their indices, i.e., $j_1 < j_2 < \dots < j_l < \dots < j_L$. Denote the interaction among factors

$1 \leq j_1 < j_2 < \dots < j_l < \dots < j_L \leq k$ as $e_{j_1 j_2 \dots j_l \dots j_L}$, with a subscript encompassing all the factors involved and with the involved factors placed in an ascending order of factor indices. As usual, $x_j = +1$ or $-1, j = 1, 2, \dots, k$. Let $r = 1, 2, \dots, n$, denote replication number. With this notation, the full regression model for 2^k factorial design can be stated as

$$y_{x_1 x_2 \dots x_k ; r} = \mu_{x_1 x_2 \dots x_k} + \varepsilon_{x_1 x_2 \dots x_k ; r} \quad (3)$$

$$\begin{aligned} \text{where } \mu_{x_1 x_2 \dots x_k} = & e_G + \sum_{1 \leq j_1 \leq k} \frac{e_{j_1}}{2} x_{j_1} + \sum_{1 \leq j_1 < j_2 \leq k} \frac{e_{j_1 j_2}}{2} x_{j_1} x_{j_2} + \sum_{1 \leq j_1 < j_2 < j_3 \leq k} \frac{e_{j_1 j_2 j_3}}{2} x_{j_1} x_{j_2} x_{j_3} \\ & + \sum_{1 \leq j_1 < j_2 < j_3 < j_4 \leq k} \frac{e_{j_1 j_2 j_3 j_4}}{2} x_{j_1} x_{j_2} x_{j_3} x_{j_4} + \dots \\ & + \sum_{1 \leq j_1 < j_2 < j_3 < \dots < j_{k-1} < j_k \leq k} \frac{e_{j_1 j_2 j_3 j_4 \dots j_{k-1} j_k}}{2} x_{j_1} x_{j_2} x_{j_3} x_{j_4} \dots x_{j_{k-1}} x_{j_k}. \end{aligned} \quad (4)$$

Note that the last term of Eq. (4) is simply $\frac{e_{1234 \dots k}}{2} x_1 x_2 x_3 x_4 \dots x_k$. Eq. (4) has 2^k equations and

2^k effects and interactions, which consist of the grand effect, k main (factor) effects and $2^k - k - 1$ interactions. Denote this entire set of grand effect, main (factor) effects and interactions as Ω .

This paper deals with the issue of identifying treatment combinations through whose experimentation model parameters, i.e., main effects and interactions, can be estimated.

Although the estimation process includes estimation of the mean responses based on experimental results, we focus only on the remainder of the estimation process and concern ourselves only with the relationship between the mean responses $\mu_{x_1 x_2 \dots x_k}$ and all the main effects and interactions. Therefore, we focus on Eq. (4) and ignore the random error term $\varepsilon_{x_1 x_2 \dots x_k ; r}$ of Eq. (3) and possible replications. Despite our focus on identifying treatment combinations with which desired main effects and interactions can be solved, deterministically, as functions of the mean responses, we nevertheless pose our problems and solutions in terms of estimation and refer to the solvability as parameter estimability. This is commonly done in the literature.

The i -th degree reduced regression model for a 2^k factorial design consists of all the summation terms on the right-hand side of Eq. (4) except those summation terms involving $i+1, i+2, \dots, k-1$ and k interactions. More precisely, it is

$$y_{x_1 x_2 \dots x_k ; r} = \mu_{x_1 x_2 \dots x_k} + \varepsilon_{x_1 x_2 \dots x_k ; r} \quad (5)$$

$$\begin{aligned} \text{where } \mu_{x_1 x_2 \dots x_k} = & e_G + \sum_{1 \leq j_1 \leq k} \frac{e_{j_1}}{2} x_{j_1} + \sum_{1 \leq j_1 < j_2 \leq k} \frac{e_{j_1 j_2}}{2} x_{j_1} x_{j_2} + \sum_{1 \leq j_1 < j_2 < j_3 \leq k} \frac{e_{j_1 j_2 j_3}}{2} x_{j_1} x_{j_2} x_{j_3} \\ & + \sum_{1 \leq j_1 < j_2 < j_3 < j_4 \leq k} \frac{e_{j_1 j_2 j_3 j_4}}{2} x_{j_1} x_{j_2} x_{j_3} x_{j_4} \dots \dots \dots \\ & + \sum_{1 \leq j_1 < j_2 < j_3 < \dots < j_{i-1} < j_i \leq k} \frac{e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}}{2} x_{j_1} x_{j_2} x_{j_3} x_{j_4} \dots x_{j_{i-1}} x_{j_i}. \end{aligned} \quad (6)$$

Note that the last term of Eq. (6) involves summation of all i -factor interactions. In other words, the only difference between the last term of Eq. (6) and the last terms of Eq. (4) is in the number of summation indices. While the last term of Eq. (6) has i summation indices (ranging from j_1

through j_i), its counterpart of Eq. (4) has k indices (symbolically ranging from j_1 through j_k and actually containing all factor indices i from 1 through k).

Denote the set of grand effect e_G as I_0 and the set of all main effects as I_1 . The set of all i -factor interactions is denoted as I_i for all i , $2 \leq i \leq k$. For ease of discussion, all the effects/interactions of an i -th degree reduced regression model 2^k are denoted as $\Omega_i \equiv I_0 \cup I_1 \cup I_2 \cup \dots \cup I_i$. $\Omega_k = \Omega$, where Ω denotes the set of all effects/interactions of a full 2^k model. For ease of discussion, the qualifier “reduced”, “regression” and “model” will be omitted in what follows when no danger of confusion exists.

We denote this i -th degree model as $2^{k,i}$, $i = 0, 1, \dots, k$. The notation i is intended as being mnemonic for interaction; the qualifier “ i -th degree” is intended for its similarity (but not equivalence) with the well-known concept of i -th degree polynomial. $2^{k,0}$ consists of only one effect, i.e., the grand effect; $2^{k,1}$ consists of $(k+1)$ effects, i.e., the grand effect and the k main (factor) effects; $2^{k,k}$ is the full regression model specified in Eq. (4).

This i -th degree model suffices if the ignored interactions are all indeed zero. Otherwise, confounding among parameter estimates may occur. Although confounding will not take place among the estimates of the i -th degree parameters (because of active confounding avoidance), it may occur between them and the ignored but actually non-zero higher-order interactions. It is often desired that estimates of i -th degree parameters are not confounded among themselves, possibly because of their importance. As a result, it is desirable that a set of treatment combinations can be identified so that their experimentation can lead to a set of non-confounded

estimates for all the i -th degree parameters. It is also desirable that the number of the identified treatment combinations is minimized and hence equal exactly to the number of unknown effects/interactions of the i -th degree model. In the next section, we define a set of treatment conditions for estimating all the effects/interactions of an i -th degree reduced model $2^{k,i}$ that achieves the least treatment-combinations, active confounding avoidance as well as forward compatibility as an i -th degree reduced design of a $2^{k,i}$ reduced factorial model and denote it as a $2^{k,i}$ design.

4. Active Confounding Avoidance Achieved by Least-Treatment-Combinations Methods

For ease of discussion, consider the 2^k equations of Eq. (4) as being ordered according to the conventional “standard order,” with the special case of 2^4 illustrated in Table 1. Eq. (4) can be written in the following matrix form:

$$\boldsymbol{\mu} = \mathbf{D}\mathbf{e}$$

where $\boldsymbol{\mu}$ is a 2^k dimensional column vector of mean responses, $\mathbf{e}$ is a 2^k -dimensional column vector of effects/interactions, and $\mathbf{D}$ is the design matrix.

Let M be any subset of Ω such that all the effects/interactions contained in $M^c \equiv \Omega \setminus M$ are 0. For convenience, we refer to those effects/interactions in M as non-zero effects/interactions, although some of them may actually be zero. Denote the cardinality of M as m . In 2^k design of experiments, mean responses are estimated first based on the results of experiments conducted for selected treatment combinations, and the effects/interactions are then estimated. With only m

non-zero effects/interactions, only m of the 2^k equations of Eq. (4) are needed to solve for the m effects/interactions. Let the m non-zero effects/interactions be denoted as $\mathbf{e}_M$. Let T_M be a set of m treatment combinations that suffices for the estimation of the m non-zero effects/interactions and let $\boldsymbol{\mu}_{T_M}$ denote the m corresponding mean responses. Moreover, let $\mathbf{D}_{T_M M}$ denote the $m \times m$ matrix relating the m mean responses $\boldsymbol{\mu}_{T_M}$ to the m non-zero effects/interactions $\mathbf{e}_M$, and let $\mathbf{D}_{T_M}$ denote the $m \times 2^k$ matrix relating the m mean responses $\boldsymbol{\mu}_{T_M}$ to the 2^k effects/interactions $\mathbf{e}$. Moreover, $\mathbf{D}_{T_M}$ can be re-organized and partitioned into two blocks $[\mathbf{D}_{T_M M}, \mathbf{D}_{T_M M^c}]$. In this notation, we have

$$\boldsymbol{\mu}_{T_M} = \mathbf{D}_{T_M M} \mathbf{e}_M \quad \text{and} \quad (7.1)$$

$$\boldsymbol{\mu}_{T_M} = \mathbf{D}_{T_M} \mathbf{e} = \begin{bmatrix} \mathbf{D}_{T_M M} & \mathbf{D}_{T_M M^c} \end{bmatrix} \begin{bmatrix} \mathbf{e}_M \\ \mathbf{e}_{M^c} \end{bmatrix} \quad (7.2)$$

Tsao and Wibowo (2005) developed a method that can be used to produce a set T_M of m treatment combinations for any given set M of effects/interactions that are to be estimated.

Problem Statement: Given any set P of p effects/interactions, find a set T_P of p treatment combinations so that (a) experiments conducted accordingly can be used to estimate the p effects/interactions if all the other effects/interactions are indeed zero and (b) their estimates are not confounded with one another if not all the other effects/interactions are zero.

Theorem 1. Let $P \subset \Omega$ be any set of p effects/interactions in a 2^k factorial experiment and let T_P be the set of p treatment combinations produced by Tsao and Wibowo (2005). Then, experiments conducted accordingly can be used to estimate the p effects/interactions if all the

other effects/interactions are indeed zero. Moreover, their estimates are not confounded with one another if not all the other effects/interactions are zero.

Proof. The first part was proved in Tsao and Wibowo (2005). By Eq. (7.1), $\mathbf{e}_P = \mathbf{D}_{T_P P}^{-1} \boldsymbol{\mu}_{T_P}$.

This specifies the estimates for the p effects/interactions. By Eq. (7.2), we have

$$\mathbf{D}_{T_P P}^{-1} \begin{bmatrix} \mathbf{D}_{T_P P} \mathbf{D}_{T_P P^c} \\ \mathbf{e}_{P^c} \end{bmatrix} = \begin{bmatrix} \mathbf{I} & \mathbf{D}_{T_P P}^{-1} \mathbf{D}_{T_P P^c} \end{bmatrix} \begin{bmatrix} \mathbf{e}_P \\ \mathbf{e}_{P^c} \end{bmatrix} = \mathbf{e}_P + \mathbf{D}_{T_P P}^{-1} \mathbf{D}_{T_P P^c} \mathbf{e}_{P^c} \quad (8)$$

This implies that when not all the other effects/interactions are zero, estimates obtained with the other effects/interactions presumed zero actually contain “contamination”, and the “contamination” is $\mathbf{D}_{T_P P}^{-1} \mathbf{D}_{T_P P^c} \mathbf{e}_{P^c}$. Note that the contamination does not involve any of the effects/interactions in P .

Corollary 1: For any 2^k factorial experiment, there exists a set of $k+1$ treatment combinations whose experimentation enables estimation of (the grand effect and) the k main effects with Resolution III.

Proof: Let P consist of the grand effect and k main effects. The conclusion follows Theorem 1 and the definition of Resolution III.

Corollary 2: For any 2^k factorial experiment, there exists a set of $k+1+(k(k-1))/2$ treatment combinations whose experimentation ensures that estimates of (the grand effect,) the k main effects and all two-factor interactions are not confounded with one another.

The proof of Corollary 2 is similar to that of Corollary 1 and is omitted. Note that the degree of confounding suffered by any design satisfying the requirement specified in Corollary 2 is no higher than a Resolution-IV design. This is because while confounding between two two-factor interactions does not occur in the former, it is allowed in the latter. Also note that the degree of confounding suffered by any such design is higher than a Resolution-V design because a main effect is allowed to be confounded with a three-factor interaction in the former but not in the latter. Theorem 1 was first reported in Tsao and Patel (2011). Corollaries 1 and 2 pertain to the estimability of the $2^{k,1}$ and $2^{k,2}$, respectively, with least treatment combinations and active confounding avoidance. Example sets of treatment combinations can be found in Tsao and Wibowo (2005) and Tsao and Liu (2008). The intuitive pattern proposed in this paper generates further examples easily, with the algorithms illustrated in Section 2 already and to be formally defined in the next section.

5. Producing $2^{k,i}$ Designs and Expanding $2^{k,i}$ to $2^{k,i+1}$ Incrementally

In this section, we first propose an algorithm called “The $2^{k,i}$ Algorithm.” It starts with an initial treatment combination and constructs on it a $2^{k,i}$ design. The initial treatment combination is set to the low (-) level for all k factors. We then propose a more detailed algorithm called “The Sequential $2^{k,i}$ Algorithm.” The difference between these two algorithms is that each iteration of the former expands a $2^{k,i}$ design directly into a $2^{k,i+1}$ design with a set of multiple treatment combinations while the latter expands a $2^{k,i}$ design into a $2^{k,i+1}$ design one treatment combination at a time. We provide the proof for the latter algorithm; the proof also establishes the validity of the former algorithm because the former is a special case of the latter.

5.1 The $2^{k,i}$ Algorithm and The Sequential $2^{k,i}$ Algorithm

The $2^{k,i}$ Algorithm produces an i -th degree reduced design $2^{k,i}$ of a 2^k factorial, for all i such that $0 \leq i \leq k$, with forward compatibility. In other words, it starts with the smallest possible reduced design consisting of only one treatment combination, for estimating the grand effect, and expands an $(i-1)$ -st degree reduced design $2^{k,i-1}$ to an i -th degree reduced design $2^{k,i}$, for all i such that $0 \leq i \leq k$. The expansion is one block at a time, with each block corresponding to the set of additional treatment combinations needed to estimate the additional parameters of an i -th degree reduced model not present in the $(i-1)$ -st degree reduced model.

The $2^{k,i}$ Algorithm (with the All-Minus Initial Treatment Combination)

Step 0: Set $i = 0$, and set $2^{k,i}$ to include only one treatment combination with the level of each of the k factors set to the low level -1 (or “-”).

Step 1: If $i = k$, stop. Otherwise, set $i = i + 1$. Set $2^{k,i}$ to $2^{k,i-1}$.

Step 2: For each of the $\binom{k}{i}$ parameters constituting I_i , perform Steps 2.1 through 2.2. Go to Step 1 afterwards.

Step 2.1: Identify the i factors involved.

Step 2.2: Add to $2^{k,i}$ the treatment combination in which the level of each of the i factors is set at the high level of +1 (or “+”) and the levels of the rest of the factors are set at the low level -1 (or “-”).

Note that in Step 2 of this Algorithm, no particular sequence of the $\binom{k}{i}$ effects/interactions in I_i is specified for performing Steps 2.1 through 2.2, and any sequence suffices. However, in the The Sequential $2^{k,i}$ Algorithm to be proposed later in this section, sequencing of the $\binom{k}{i}$ effects/interactions in I_i is important, and the sequence will be specified by the experimenter. In addition, the sequence in which additional treatment conditions are incrementally added for expansion from $2^{k,i}$ to $2^{k,i+1}$ is important. These two types of corresponding sequencing constitute the key and only difference in the two algorithms.

We now consider the problem of expanding an i -th degree reduced design $2^{k,i}$ to an $(i+1)$ -st degree reduced design $2^{k,i+1}$ one treatment combination at a time so that, with each additional treatment combination, one more effect/interaction in any given sequence of importance, e.g., non-increasing order of magnitude among all i -factor interactions, can be estimated. As usual, the estimation is required to be such that no confounding exists among the effects/interactions being estimated explicitly, and the number of treatment conditions required is minimum and hence equal exactly to the number of effects/interactions being estimated. We propose an algorithm for such expansion and refer to it as “The Sequential $2^{k,i}$ Algorithm.”

Assume that, for each i , $1 \leq i \leq k$, the $\binom{k}{i}$ parameters constituting I_i are sequenced according to a non-ascending order of their importance, e.g., their magnitude. Denote the sequenced set as $\underline{I}_i$. In addition, $2^{k,i}$ is now considered an ordered set. With this notation and terminology, we state The Sequential $2^{k,i}$ Algorithm as follows:

The Sequential $2^{k,i}$ Algorithm (with the All-Minus Initial Treatment Combination)

Step 0: Set $i = 0$, and set $2^{k,i}$ to include only one treatment combination with the level of each of the k factors set to the low level -1 (or “-”).

Step 1: If $i = k$, stop. Otherwise, set $i = i+1$. Set the ordered set $2^{k,i}$ to the ordered set $2^{k,i-1}$.

Step 2: For each of the $\binom{k}{i}$ parameters constituting I_i , perform Steps 2.1 through 2.2 according to the sequence specified in I_i . Go to Step 1 afterwards.

Step 2.1: Identify the i factors involved.

Step 2.2: Expand the ordered set $2^{k,i}$ with the treatment combination in which the level of each of the i factors is set at the high level of +1 (or “+”) and the levels of the rest of the factors are set at the low level -1 (or “-”).

Since “The $2^{k,i}$ Algorithm” is a degenerate version of the “The Sequential $2^{k,i}$ Algorithm,” it suffices to provide a proof of the latter.

Denote the ordered set of treatment combinations generated for $2^{k,i}$ as $\Phi_{k,i}$ and the corresponding ordered set of mean responses as $\Psi_{k,i}$. The square matrix associated with a $2^{k,i}$ reduced models and a corresponding $2^{k,i}$ design are of particular importance in the proofs. We refer to such a matrix as the design matrix of the $2^{k,i}$ reduced model and its corresponding $2^{k,i}$ design. For ease of discussion, we will refer to such a matrix simply as the design matrix of a $2^{k,i}$

design or simply as a $2^{k,i}$ design matrix. Let $\overline{\omega}_i$ denote the number of parameters in a $2^{k,i}$ reduced model, and

$$\overline{\omega}_i = \binom{k}{0} + \binom{k}{1} + \binom{k}{2} + \dots + \binom{k}{i-1} + \binom{k}{i} = \sum_{l=0}^i \binom{k}{l}.$$

A $2^{k,i}$ design matrix is therefore a $\overline{\omega}_i \times \overline{\omega}_i$ matrix.

5.2 The Estimation Strategy

Suppose that a $2^{k,i-1}$ design has been found for the $2^{k,i-1}$ model. It turns out that any i -factor interaction $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ of a $2^{k,i}$ model can be directly estimated with a simple linear function of the mean responses of the $2^{k,i-1}$ model and the mean response of only one new treatment combination beyond the $2^{k,i-1}$ design. In fact, this new treatment combination is closely related to the i -factor interaction being estimated and is such that factors $j_1, j_2, \dots, j_{i-1}$ and j_i are all set to the high level (i.e., “+1” or “+”) and all the other factors are set to the low level (i.e., “-1” or “-”).

This treatment combination can be expressed in general as

$-1, \dots, -1, x_{j_1} = 1, -1, \dots, -1, x_{j_i} = 1, -1, \dots, -1$. Given the treatment combinations of the $2^{k,i-1}$ design, this treatment combination completes a full factorial for all the factors involved in the i -factor interaction being estimated, i.e., factors $j_1, j_2, \dots, j_{i-1}$ and j_i . Note the complete symmetry between the i factors involved in the i -factor interaction $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ being estimated and the factors which are set to the high level in this new treatment combination.

Our strategy for estimating $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ consists of three steps:

- Select one additional treatment combination where factors $j_1, j_2, \dots, j_{i-1}$ and j_i are all set to the high level (i.e., “+1” or “+”) and all the other factors are set to the low level (i.e., “-1” or “-”).
- Identify the treatment combinations of the $2^{k,i-1}$ design that, together with this new treatment combination, constitute a full factorial for the factors.
- Focus on exclusively those rows in the $2^{k,i}$ design matrix corresponding to these treatment combinations and the companion mean responses. Obtain the coefficients of $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ associated with all these treatment combinations (of the full factorial for the i factors). Set the estimator $f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$ of this interaction $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ to be the inner product of the coefficients of the $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ just obtained and the corresponding mean responses, divided by the divisor 2^{i-1} . $f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$ is a linear combination of the mean responses associated with the treatment combinations of $2^{k,i}$. Note however that in a $2^{k,i}$ model, the mean responses, i.e., the μ ’s, are expressed as functions of only parameters in Ω_i . As a result, this estimator function $f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$ is a function of the parameters in Ω_i .

Let $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ be the i -factor interaction being estimated. The linear combination can be obtained from the $2^{k,i-1}$ design matrix and the new treatment combination with the i factors set to the high level as follows:

$$f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i}) \equiv \frac{f'_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})}{2^{i-1}} \quad (9)$$

where 2^{i-1} is the usual divisor and

$$\begin{aligned}
f'_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i}) &\equiv (-1)^{i-0} \mu_{-1, -1, \dots, -1, -1} \\
&+ (-1)^{i-1} \sum_{u_1 \in \{j_1, j_2, j_3, j_4, \dots, j_{i-1}, j_i\}} \mu_{-1, \dots, -1, x_{u_1}=1, -1, \dots, -1} \\
&+ (-1)^{i-2} \sum_{\{u_1, u_2 | u_1 < u_2\} \subset \{j_1, j_2, j_3, j_4, \dots, j_{i-1}, j_i\}} \mu_{-1, \dots, -1, x_{u_1}=1, -1, \dots, -1, x_{u_2}=1, -1, \dots, -1} \\
&+ \dots \\
&+ (-1)^{i-(i-1)} \sum_{\{u_1, u_2, \dots, u_{i-1} | u_1 < u_2 < \dots < u_{i-1}\} \subset \{j_1, j_2, j_3, j_4, \dots, j_{i-1}, j_i\}} \mu_{-1, \dots, -1, x_{u_1}=1, -1, \dots, -1, x_{u_{i-1}}=1, -1, \dots, -1} \\
&+ (-1)^{i-i} \mu_{-1, \dots, -1, x_{j_1}=1, -1, \dots, -1, x_{j_i}=1, -1, \dots, -1}
\end{aligned} \tag{10}$$

Note that all the mean responses involved in Eq. (9) are associated with treatment combinations already obtained in $2^{k,i-1}$, with only one exception. The exception is the last mean response $\mu_{-1, \dots, -1, x_{j_1}=1, -1, \dots, -1, x_{j_i}=1, -1, \dots, -1}$, and this mean response corresponds to the treatment combination chosen as the one additional treatment combination beyond the $2^{k,i-1}$ design to be used for estimating $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$.

Note also that this function does not involve any treatment combination in which at least one factor not belonging to the set of factors $j_1, j_2, \dots, j_{i-1}$ and j_i is set to the high level. This means that all the treatment combinations involved constitute a full factorial design for the i factors $j_1, j_2, \dots, j_i$ and that the levels for all the other factors are set at the low level (i.e., “-”).

5.3 Proofs

Theorem 2: Suppose that $2^{k,i-1}$ is an $(i-1)$ -st degree reduced design. The linear combination

$f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$, as defined in Eq. (9), of the mean responses of $2^{k,i-1}$ and the mean response

$\mu_{-1, \dots, -1, x_{j_1}=1, -1, \dots, -1, x_{j_i}=1, -1, \dots, -1}$ of the treatment combination

$-1, \dots, -1, x_{j_1}=1, -1, \dots, -1, x_{j_i}=1, -1, \dots, -1$ produces exactly the interaction $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ of the i

factors $j_1, j_2, \dots, j_{i-1}$ and j_i . This fact is independent of whether any other i -factor interaction

precedes $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in the magnitude order specified by the experimenter and hence whether a

treatment combination has been identified for any other i -factor interaction accordingly.

Proof: Each of the mean responses in Eq. (9) can be replaced with a linear combination of the

parameters of $2^{k,i-1}$ and all the i -factor interactions preceding $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in the experimenter's

parameter sequence of non-increasing magnitude. To show that $f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$ produces

exactly $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ regardless of the experimenter's sequence, we replace each of the mean

responses in Eq. (9) with a linear combination of all the parameters of $2^{k,i}$, including all $\binom{k}{i}$ i -

factor interactions. We show that, with this “robust” replacement, the coefficient of

$e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in Eq. (10) is 2^i and the coefficients for all the other parameters, including those i -

factor interactions succeeding $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in the experimenter's parameter sequence, is 0.

Note that the treatment combinations involved in $f_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}(\Psi_{k,i})$ constitute a full factorial for the i factors, with the levels of all other factors set at low (“-”); no other treatment combinations are involved. Moreover, the coefficients of the mean responses in Eq. (10) are exactly the corresponding entries in the $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ column of the full 2^k design matrix. Therefore, Eq. (10) is nothing but the inner product of the $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ column and the mean response column, with the scope limited to only those treatment combinations constituting a full factorial for the i factors. This implies that the coefficient of $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in Eq. (10) is 2^i . In the rest of this proof, we will limit our attention to only those treatment combinations constituting a full factorial for the i factors. For ease of discussion, when we refer to a column, we actually address only those entries whose corresponding rows constituting the full factorial for the i factors. Similarly, when we refer to a full design matrix, we actually address only those rows whose corresponding treatment combinations constitute the full factorial for the i factors.

The other parameters, including all parameters of a $2^{k,i}$ but excluding $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$, can be partitioned into two groups. Group 1 is the set of all the parameters of a full factorial of the i factors $j_1, j_2, \dots, j_{i-1}$ and j_i , except $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$; these parameters include all main effects of the i factors $j_1, j_2, \dots, j_{i-1}$ and j_i , all interactions between any two of these i factors, and up to all interactions among any $i-1$ factors of these i factors. Group 2 consists of all the other parameters. Note that Group 2 contains all i -factor interactions other than $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$, and the reasoning below applies to all these i -factor interactions. We deal with group 1 first and then group 2. The orthogonality among all columns of this full design matrix (associated with only the i factors $j_1, j_2, \dots, j_{i-1}$ and j_i) implies that in Eq. (10), the coefficients for all the parameters of

group 1 is 0. Group 2 parameters can be further partitioned into two sub-groups: those involving at least one of the i factors $j_1, j_2, \dots, j_{i-1}$ and j_i and those involving no such factors. The column associated with any parameter of the first sub-group is obtained by multiplying the levels of those factors belonging to the set of factors $j_1, j_2, \dots, j_{i-1}$ and j_i by a constant -1 or 1 depending on whether there are an odd or even number of other factors involved in the parameter. The orthogonality among the columns of the full factorial of $j_1, j_2, \dots, j_{i-1}$ and j_i ensures the orthogonality between this column and the column associated with $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$. The orthogonality between the column associated with any parameter of the second sub-group and the $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ column results from the fact that the coefficients of the former column are identically -1 or 1, depending on whether there are an odd or even number of other factors involved in the parameter, and the fact that the coefficients of the latter column sum up to 0. Since the above reasoning is made with all i -factor interactions included in substituting the mean responses, these established facts are independent of whether or not any other i -factor interaction precedes $e_{j_1 j_2 j_3 j_4 \dots j_{i-1} j_i}$ in the magnitude order specified by the experimenter and hence whether or not a treatment combination has been identified for any other i -factor interaction accordingly. This completes the proof.

Theorem 3: Applying The Sequential $2^{k,i}$ Algorithm expands an $(i-1)$ -st degree design to an i -th degree reduced design, for all i such that $1 \leq i \leq k$, one treatment combination at a time so that, with each additional treatment combination, one more effect/interaction in any given sequence of importance, e.g., non-ascending order of magnitude among all i -factor interactions, can be estimated.

Proof: We prove this theorem by mathematical induction. We first establish the theorem for the 1st degree reduced design (for the 1st degree reduced regression model) and then use mathematical induction over the design degree, with a discussion focused on the scope expansion from $(i-1)$ -factor interactions to i -factor interactions one treatment combination at a time. It is trivial to see that the initial treatment combination suffices for estimation of the only effect e_G of the 0-th degree reduced model $2^{k,0}$. Denote the k main effects of the ordered set $\underline{I}_1$ as $e_{g(s)}$ where $s, s = 1, 2, \dots, k$, denotes the order and the function $g(s)$ denotes the s -th factor in $\underline{I}_1$. Let us focus on any arbitrary $t, t = 1, 2, \dots, k$. The task is to show that the first t treatment combinations generated by the Sequential $2^{k,i}$ Algorithm (together with the given initial treatment combination) can be used to estimate the first t main effects of $\underline{I}_1$. The reduced model for the case where main effects $e_{g(s)}$ for $s = t+1, \dots, k$, are zero is simply

$$\mu_{-1,-1,-1,\dots,-1} = e_G + \sum_{u=1}^t \left(-\frac{e_{g(u)}}{2} \right), \quad (11)$$

$$\mu_{-1,-1,x_{g(s)=1},-1,\dots,-1} = e_G + \sum_{u=1}^{s-1} \left(-\frac{e_{g(u)}}{2} \right) + \frac{e_{g(s)}}{2} + \sum_{u=s+1}^t \left(-\frac{e_{g(u)}}{2} \right), \text{ for } s=1,2,\dots,t. \quad (12)$$

Note that the order of effects/interactions appearing on the right-hand sides of these equations corresponds to the sequence of the effects/interactions specified in $\underline{I}_1$ and that the order of the equations corresponds to the sequence of treatment combinations specified by The Sequential $2^{k,i}$ Algorithm. It is clear that $e_{g(s)}$ can be solved, for each $s=1,2,\dots,t$, and is equal to

$\mu_{-1,-1,x_{g(s)=1},-1,\dots,-1} - \mu_{-1,-1,-1,-1,\dots,-1}$. Once all $e_{g(s)}$ are estimated, e_G can be easily estimated with Eq.

(11) or any of the t equations of Eq. (12). Note that the estimation of each $e_{g(s)}$ depends on the

treatment combinations already identified for the reduced design of one fewer degree, i.e., the sole treatment combination with all factors set to their low (-) levels already identified for the $2^{k,0}$ reduced design in this particular case, and only one treatment combination beyond. Also note that this is true for $t = 1, 2, \dots, k$, and hence we have established the theorem for up to the $2^{k,1}$ reduced design. In addition, the set of $(k+1)$ treatment combinations of the (ordered) $2^{k,1}$ reduced design is the same as the (non-ordered) $2^{k,1}$ reduced design that is generated with The $2^{k,i}$ Algorithm. This implies that this $\varpi_1 \times \varpi_1 = (1+k) \times (1+k)$ $2^{k,1}$ design matrix is non-singular. This will be the basis for the mathematical induction.

Now, assume that all the parameters in $\underline{I}_{i-1}$ can be estimated with the $(i-1)$ -st degree design $2^{k,i-1}$; denote this $\varpi_{i-1} \times \varpi_{i-1}$ $2^{k,i-1}$ design matrix as M_{i-1} . This implies that M_{i-1} is non-singular.

As the parameters of I_i are added to the model, one after another, and as the corresponding treatment combinations are added to the design, the square design matrix grows from a

$\varpi_{i-1} \times \varpi_{i-1}$ matrix to a $\varpi_i \times \varpi_i$ matrix. Now, focus on the addition to the model of the t -th i -

factor interaction in $\underline{I}_i$, $t = 1, 2, 3, \dots, \binom{k}{i}$. Assume, of course, an arbitrary sequence $\underline{I}_i$ of the

$\binom{k}{i}$ i -factor interactions.

Denote the $(\varpi_{i-1} + t) \times (\varpi_{i-1} + t)$ design matrix as $M_{i-1,t}$. Denote the first ϖ_{i-1} rows of $M_{i-1,t}$

as $M_{i-1,t}^{i-1}$; it is a $\varpi_{i-1} \times (\varpi_{i-1} + t)$ matrix. We need to prove that design matrix $M_{i-1,t}$ is non-

singular. We show this in two steps. The first step shows that each of the t i -factor interactions

can be estimated; step two starts with substitution of these t estimates into the $\varpi_{i-1} \times (\varpi_{i-1} + t)$

matrix $M_{i-1,t}^{i-1}$, reducing the question of estimability of those ϖ_{i-1} parameters of

$\Omega_{i-1} \equiv I_0 \cup I_1 \cup I_2 \cup \dots \cup I_{i-1}$ to the question of invertibility of the $\varpi_{i-1} \times \varpi_{i-1} 2^{k,i-1}$ design matrix M_{i-1} .

Invoking the induction hypothesis concludes the step. Note that the first ϖ_{i-1} columns of $M_{i-1,t}^{i-1}$

is M_{i-1} . Denote the remainder of $M_{i-1,t}^{i-1}$ as $M_{i-1,t}^t$. Therefore, we have $M_{i-1,t}^{i-1} \equiv [M_{i-1} M_{i-1,t}^t]$.

Let $e_{j_1(s), j_2(s), \dots, j_{i-1}(s), j_i(s)}$, where $s, s = 1, 2, 3, \dots, \binom{k}{i}$, denote the s -th i -factor interaction of the

sequence and the composite subscript $j_1(s), j_2(s), \dots, j_{i-1}(s), j_i(s)$ denote the i factors involved in the s -th

interaction, with the convention of $1 \leq j_1(s) < j_2(s) < \dots < j_{i-1}(s) < j_i(s) \leq k$. By Theorem 2,

$f_{j_1(s), j_2(s), \dots, j_{i-1}(s), j_i(s)}(\Psi_{k,i})$ produces, for each $s = 1, 2, 3, \dots, \binom{k}{i}$, exactly $e_{j_1(s), j_2(s), \dots, j_{i-1}(s), j_i(s)}$,

regardless of the sequence. Therefore, the estimability of $e_{j_1(s), j_2(s), \dots, j_{i-1}(s), j_i(s)}$ for all

$s = 1, 2, 3, \dots, t$ is established. Now, the relationship $M_{i-1,t}^{i-1} \equiv [M_{i-1} M_{i-1,t}^t]$ implies that the

estimability of the ϖ_{i-1} parameters of $\Omega_{i-1} \equiv I_0 \cup I_1 \cup I_2 \cup \dots \cup I_{i-1}$ depends on whether M_{i-1} is

invertible or not. But, this invertibility is simply the induction hypothesis. This completes the proof.

Note that, in the context of Theorem 3, although estimates of i -factor interactions will not change when additional i -factor interactions are estimated, estimates of the main effects and interactions involving $i-1$ or fewer factors will change. Therefore, estimating one more i -factor interaction actually requires estimation/re-estimation of all the main effects and all interactions involving $i-1$

or fewer factors that are included in the current model. We state the following corollary about this estimation/re-estimation. The proof is straightforward and hence omitted.

Corollary 3: In the estimation/re-estimation performed in the context of Theorem 3 when one additional main effect or interaction is included in the expanded model and the corresponding treatment combination is included in the expanded design, no confounding exists among the estimates of the effects/interactions of the expanded model. In addition, the number of treatment combinations is minimum and equal exactly to the number of effects/interactions of the expanded model. Moreover, all the sequentially expanding designs are forward-compatible.

Both The $2^{k,i}$ Algorithm and The Sequential $2^{k,i}$ Algorithm proposed in the previous section start with the all-minus initial treatment combination, i.e., the treatment combination in which all factors are set to their low levels. This is not necessary. In fact, the initial treatment combination can be any arbitrary treatment combination.

This is because the low and the high levels of a factor can be and is often designated arbitrarily and the current designations may be reversed without affecting the properties about effect/interaction estimability and with active confounding avoidance remaining intact. Level designation for any of the factors can be reversed, if necessary, so that the initial arbitrary treatment combination is mapped into a new label consisting of low levels for all factors. With such a reversal, the sign of the corresponding main effect should be reversed as well. In addition, the signs of interactions involving an odd number of factors whose level designation is

reversed should be reversed as well. Despite the sign changes, the properties about effect/interaction estimability and active confounding avoidance remain intact.

6. Applications and Comparisons

In this section, we briefly discuss several applications of the proposed $2^{k,i}$ reduced models and the proposed simple design pattern useful for sequential and incremental expansion of a $2^{k,i}$ reduced model to the next larger $2^{k,i+1}$ reduced model, all with least treatment combinations and active confounding avoidance. We also compare prevailing methods to the proposed methods and point out our contributions. In particular, we discuss the following five aspects individually: least treatment combinations, active confounding avoidance, forward compatibility, the simple design pattern, and sequential and incremental expansion. The unique advantages of the proposed methods about $2^{k,i}$ result from the simultaneous occurrence of the advantages of first four of these five aspects. The unique advantages of the proposed methods about sequential expansion from $2^{k,i-1}$ to $2^{k,i}$ result from the simultaneous occurrence of the advantages of all these five aspects. A comparison between the proposed method and the concept of optimal design, particularly the D-optimality, will be provided at the end of this section.

The numbers of treatment combinations required for all prevailing 2^k designs, including the classical fractional factorial designs (Montgomery, 2009), the Plackett-Burman designs (Montgomery, 2009), the Taguchi orthogonal-array designs (Taguchi and Konishi, 1987), are multiples of an integer, e.g., 4. Often, two such neighboring numbers of a method may be quite

far from each other, e.g., with a gap of 8 between 2^{5-1} and 2^{5-2} . When the experimenter has prior knowledge about the identities of significant effects and interactions, based on domain knowledge or past empirical data, the number of treatment combinations required by these methods for estimating the significant effects and interactions may be larger than necessary. This is a major issue for experiments that require a large amount of resources or a long time. The least-treatment-combinations approach first proposed in Tsao and Wibowo (2005) and adopted in this work achieves minimization of experimental resources.

The prevailing methods produce specific designs, whose levels of resolution may or may not be easy to decipher. While the resolution level of a classical fractional factorial design can be determined with the simple systematic method of aliasing, determining the resolution level of a Plackett-Burman design or a Taguchi orthogonal-array design may require a numerical algorithm. The typical process of selecting a design involves comparing several candidate designs, each with a particular resolution level and even an aberration level, and selecting one with the highest resolution and lowest aberration. Active confounding avoidance is a different approach; with any pre-determined set of significant effects and interactions whose estimates should not be confounded, it actively seeks a set of treatment combinations that ensure absence of any confounding between any pair of the significant effects and interactions. Straightforward applications of this approach include the following. While the prevailing methods do provide saturated designs (of resolution III), in which all main effects can be estimated without confounding among themselves, they only work for experiments involving k factors such that $k+1$ is a multiple of 4 (Montgomery, 2009). However, the $2^{k,1}$ reduced model, a special case of the $2^{k,i}$ model proposed in this paper, consists of only the grand effect and all k main effects, and

the proposed $2^{k,i}$ Algorithm produces a saturated design for any number of factors k , whether $k+1$ is a multiple of 4 or not. In addition, a resolution IV design allows confounding between two two-factor interactions, and this confounding is often undesirable. The proposed $2^{k,2}$ reduced model consists of only the grand effect, all k main effects and all the $\binom{k}{2}$ two-factor interactions, and the active confounding avoidance feature of the proposed $2^{k,i}$ Algorithm ensures that the (minimal) set of treatment combinations identified by the algorithm produces a set of estimates of the $\binom{k}{2} + k + 1$ significant effects/interactions that are not confounded with one another at all.

Moreover, in a resolution V design, confounding between a main effect and a three-factor interaction is not allowed. Since a three-factor interaction is often considered insignificant or non-existent in many experiments, this disallowance may not be desirable. A $2^{k,2}$ reduced design produced by The $2^{k,i}$ Algorithm allows it while disallowing any confounding between any two two-factor interactions, which is the main concern leading to the use of a resolution V design. These advantages also point out the possibility that, given the new concept of active confounding avoidance, the concept of resolution may not be a “high-resolution” concept after all.

The concept of forward compatibility does not seem to be present in the prevailing methods. Although the techniques of adding another fraction and folding over in the classical fractional factorial design are consistent with forward compatibility, they necessitate doubling of the number of treatment combinations and hence operate at the fraction level. Our concept of forward compatibility operates at the level of individual model parameter, i.e., at the level of an effect/interaction. In the classical fractional factorial approach, good or perhaps best designs are often given in table formats. For example, a good and perhaps the best resolution III 2^{6-3}

fractional factorial design is generated with the aliases of $D=AB$, $E=AC$, $F=BC$ while a good and perhaps the best resolution IV 2^{6-2} fractional factorial design is generated with the aliases of $E=ABC$, $F=BCD$ (e.g., Montgomery, 2009). However, since not all the treatment combinations of the former design are in the latter design, not all the experimental results obtained in the former experiment can be reused in the latter. As a result, to implement the latter design beyond the former, more than 2^{6-3} additional treatment combinations would have to be experimented. The methods we propose in this paper address this issue of forward compatibility explicitly and achieve it directly.

While numerical algorithms have been proposed to seek optimal designs of various sorts, e.g., Mee (2004) and Bulutoglu and Ryan (2009), we provide a simple design pattern that can be used by inspection to obtain a minimal set of treatment combinations for estimating all the effects and interactions of a $2^{k,i}$ reduced model. Moreover, the simple design pattern can also be used by inspection to expand a $2^{k,i}$ reduced design to a $2^{k,i+1}$ reduced design one additional treatment combination at a time for estimating one additional effect or interaction. No look-up in design tables or use of numerical algorithm is needed at all. In addition, although the layout of treatment combinations in a conventional design matrix, i.e., in the “standard order,” facilitates exhaustive listing of all possible combinations, the layout proposed in this paper, as illustrated in Table 3, informs the user of the table which one additional treatment combination enables estimation of which one additional parameter, i.e., effect or interaction, of the model. In fact, the layout proposed in this paper, as illustrated in Table 3, is another easy way to exhaustively list all possible combinations. What we have proposed is a design pattern from which a specific design or layout can be intuitively and easily generated according to the relative importance or

magnitude of all the effects/interactions in the mind of the experimenter. Any such specific layout may be considered to be in “importance order.” To clearly show the descending (or non-increasing) order of the effect/interaction importance for which such a “importance-order layout” is generated, the (effect/interaction) columns should be ordered to exhibit the decreasing (or non-increasing) effect/interaction importance, as illustrated in Tables 2 and 4.

Recall that this paper deals with estimability of parameters, not with the estimation accuracy; analysis of estimation accuracy requires knowledge of the sample size for each treatment combination, among other things. However, we briefly address the issue of estimation precision, which can be regarded as estimation accuracy only when the parameter is estimable and the estimator is unbiased. Our discussion is focused on the important concept of optimal design, particularly the D -optimality in the context of 2^k factorial design. Given a range for each of the p design variables (typically as coded variables ranging from -1 through +1), a fixed number n of experimental runs and the corresponding set of n regression equations $\mathbf{Y} = \mathbf{X}\boldsymbol{\beta} + \boldsymbol{\varepsilon}$, a set of design points is said to be D -optimal if the $|\mathbf{X}'\mathbf{X}|$ determinant achieves the maximum possible value, so that the “volume” of the p -dimensional confidence region associated with the estimator $\hat{\boldsymbol{\beta}}$ is minimized. Any individual design, as part of any sequence of designs proposed in this paper, may or may not be D -optimal or nearly D -optimal. Box and Draper (1971) pointed out early on, ‘One possible disadvantage of the $|\mathbf{X}'\mathbf{X}|$ criterion is that it is a “variance criterion” and effectively assumes that the model considered is the true model. As was discussed in a series of papers (beginning with Box and Draper 1959, 1963) bias error, which arises from the fact that the model rarely is absolutely correct, has usually a far greater effect on design choice than does variance error when the design is unrestricted. In situations where the design is physically

restricted to (say) a small spherical or (as here) a small cuboidal region of interest, the difference between the spread of the design points for the best all-bias design and for the best all-variance design is often not large simply due to the physical circumstances (see Stigler (1970)). The theory given by Box and Draper (1959) is, however, still applicable. The $|X'X|$ criterion, then, appears to be not unrealistic either when the model is correct or when the design is restricted to the region of interest, or both.' Steinberg and Hunter (1984) also pointed out inference precision as the motivation of the optimal design. We in this paper are concerned mainly with iterative identification of an adequate and parsimonious model, to help the experimenter throughout the exploratory process.

Mathematical theories, algorithms and software tools have been developed to search for D -optimal designs, e.g., Kiefer and Wolfowitz, 1959; Kiefer and Wolfowitz, 1960; St. John and Draper, 1975; Mitchell, 1974; Welch, W.J., 1982; Bulutoglu and Ryan, 2009. However, true D -optimality cannot be guaranteed because of the combinatorial and non-convexity nature of the mathematical problem and the resulting existence of multiple local maxima. Algorithms and software tools have also been developed to augment an initial design with more design points for improvement in estimation precision of the current model parameters and/or for estimability of more effects/interactions, all with the goal of D -optimality (e.g., Evans, 1979; Verotta, 1988; SAS, 2010). Such augmentation has been referred to as “repairing the initial design” (Evans, 1979). Such “repairing” can be conducted iteratively with a starting design of only one design point (for only one parameter) and with one additional design point (for one additional parameter) in each “repair,” hence mimicking the dual sequencing of parameters and treatment combinations proposed in this paper and Tsao and Liu (2008). However, these repeated

“constrained” D -optimization processes can no longer ensure D -optimality for any of the designs (Verotta, 1988).

The optimal sequential designs first proposed in Tsao and Liu (2008) for incremental model building are relative new, and the authors are not aware of any published literature about extension of the classical D -optimality concept to this context of sequential experimentation where overall inference precision throughout the incremental model-building process should be the main concern, rather than that of any one individual intermediate design. The authors’ research on this extension is ongoing and their findings will be reported separately.

7. Concluding Remarks

The concept of least treatment combinations was first developed in Tsao and Wibowo (2005); we refer to it as such in this paper. The concept of active confounding avoidance was first developed in Tsao and Patel (2011); we refer to it as such in this paper. The concept of a $2^{k,i}$ reduced model proposed in this paper provides a new way to specify important sets of unknown effects and interactions; the concept of a $2^{k,i}$ reduced design accentuates the importance of resource-requirement minimization, in terms of minimizing the number of treatment combinations, while improving the estimation accuracy via active confounding avoidance.

While these concepts offer several major theoretical advantages, the simple design pattern, The $2^{k,i}$ Algorithm and their generalized counterparts proposed in this paper provide a simple way to harness all the theoretical advantages. The concept of forward compatibility was first developed

in Tsao and Liu (2008). The concept of sequential expansion of a $2^{k,i}$ reduced design to a $2^{k,i+1}$ proposed in this paper further extends the aforementioned theoretical advantages of minimum resource requirement and estimation accuracy throughout the entire experimental process. We note, however, that such one-treatment-combination-at-a-time sequential expansion should not be implemented without due consideration of run-order randomization. Although such or any other run sequencing may not be fully compatible with run-order randomization, run sequencing is common and often necessary, particularly when experimentation is expensive and time consuming. In the larger context of experimentation planning, Montgomery (2009) suggests that experimentation should be conducted iteratively and sequentially, and the initial design, which is often intended for gaining experience and learning, should not consume more than 25% to 30% of the budget. To the experimenter, the sequential expansion proposed in this paper is optimal in the sense that the experimentation can stop whenever the current model is deemed adequate and no experiments already conducted could be considered unnecessary. Worthy future work includes extensions of the proposed concepts and methods to deal with experimental contexts in which blocking is important as well. On the proposed sequential expansion of a $2^{k,i}$ reduced design to a $2^{k,i+1}$ reduced design, a valuable topic for future research is balanced consideration for run-order randomization. Our research on integration of the proposed methods with the classical concept of D -optimality is underway.

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Table 1: Full Design Matrix Facilitating Parameter Estimation

	G	A	B	C	D	AB	AC	AD	BC	BD	CD	ABC	ABD	ACD	BCD	ABCD	M.R.
TC1	1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1	μ_1
TC2	1	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	μ_2
TC3	1	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1	μ_3
TC4	1	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1	μ_4
TC5	1	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1	μ_5
TC6	1	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1	μ_6
TC7	1	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1	μ_7
TC8	1	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1	μ_8
TC9	1	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1	μ_9
TC10	1	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1	μ_{10}
TC11	1	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1	μ_{11}
TC12	1	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1	μ_{12}
TC13	1	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1	μ_{13}
TC14	1	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1	μ_{14}
TC15	1	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1	μ_{15}
TC16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	μ_{16}
Divisor	16	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	

Table 2: The Intuitive Design Pattern for $2^{4,0}$, $2^{4,1}$, $2^{4,2}$, $2^{4,3}$ and $2^{4,4} = 2^4$: Full Design Matrix

	G	A	B	C	D	AB	AC	AD	BC	BD	CD	ABC	ABD	ACD	BCD	ABCD
TC1	1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
TC2	1	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
TC3	1	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1
TC5	1	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
TC9	1	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
TC4	1	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1
TC6	1	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1
TC10	1	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1
TC7	1	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1
TC11	1	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1
TC13	1	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
TC8	1	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
TC12	1	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
TC14	1	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1
TC15	1	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1
TC16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Table 3: The Intuitive Design Pattern for $2^{4,0}$, $2^{4,1}$, $2^{4,2}$, $2^{4,3}$ and $2^{4,4} = 2^4$: Treatment Combinations (with the Label and Abbreviation TC Omitted for Clarity)

----	1
+---	2
-+--	3
--+-	5
---+	9
++--	4
+--+	6
+--+	10
-++-	7
-++-	11
--++	13
+++-	8
++-+	12
+---+	14
-+++	15
++++	16

Table 4. Estimating ABC of $2^{4,3}$ First: Illustration of the Estimation Process

	G	A	B	C	D	AB	AC	AD	BC	BD	CD	ABC	m.r.
TC1 ----	1	-1	-1	-1	-1	1	1	1	1	1	1	-1	μ_1
TC2 +----	1	1	-1	-1	-1	-1	-1	-1	1	1	1	1	μ_2
TC3 --+--	1	-1	1	-1	-1	-1	1	1	-1	-1	1	1	μ_3
TC5 ---+-	1	-1	-1	1	-1	1	-1	1	-1	1	-1	1	μ_5
TC9 ----+	1	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	μ_9
TC4 ++--	1	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	μ_4
TC6 +-+-	1	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	μ_6
TC10 +--+	1	1	-1	-1	1	-1	-1	1	1	-1	-1	1	μ_{10}
TC7 -++-	1	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	μ_7
TC11 -+++	1	-1	1	-1	1	-1	1	-1	-1	1	-1	1	μ_{11}
TC13 ---++	1	-1	-1	1	1	1	-1	-1	-1	-1	1	1	μ_{13}
TC8 +++-	1	1	1	1	-1	1	1	-1	1	-1	-1	1	μ_8