Sequential Synthesis of Nanomaterials via Level-expansion

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Abstract

Nanotechnology is forging era-defining breakthroughs across science and engineering. In particular, one-dimensional nanostructures such as nanowires, nanotubes and nanobelts are widely regarded as critical building blocks for creating the next generation of devices in electronics, optics, energy and biomedicine. Motivated by a practical problem of sequential synthesis of nanowires, we propose a new statistical design augmentation method, called *level-expansion*. For a fractional factorial design at two levels, this method creates a follow-up design by expanding some of the factors in the initial design to four elaborately chosen levels and reversing the signs of the remaining factors.

The augmented design produced as such strikes a fine balance between dealiasing and entertaining nonlinear effects. Some statistical properties of the proposed method are derived. The effectiveness of the proposed method is successfully illustrated with a case study for growing a new type of zinc-oxide nanowire. The use of level-expansion in the case study unveils some previously unknown nonlinear relationships between the concentration of polyethyleneimine and the length of nanowires. This finding is important for nanoscientists to invent new zinc-oxide nanowires with better macroscopic transport properties. The proposed method is very general. Besides nanotechnology, it applies broadly to problems in many other scientific fields with similar traits where a follow-up design is needed for the dual purposes of investigating nonlinear effects and dealising.

1 INTRODUCTION

Nanotechnology is bringing about era-defining breakthroughs in science and engineering. This field studies materials and structures of 100 nanometers or smaller, where 1 nanometer $= 10^{-9}$ meter. In particular, one-dimensional nanostructures, such as nanowires, nanotubes and nanobelts, possess unique macroscopic transport properties and are widely regarded as critical building blocks for developing advanced devices in fields as varied as electronics, optics, mechanics and thermoelectrics (Venkatasubramanian et al., 2001; Patolsky et al., 2007; Wang et al., 2008; Hochbaum and Yang, 2009). For illustration, Figure 1 presents three types of ZnO nanomaterials with different splendid forms. The current research on nanosynthesis is shifting from discovery of new morphology to input controllability and reproducibility (Wang et al., 2007).

Recently, statistical methods have started making inroads into nanotechnology. Dasgupta et al. (2008) developed new statistical models to link the probabilities of obtaining specific morphologies to process variables. Deng et al. (2009) proposed a statistical technique, called sequential profile adjustment by regression, to produce precise estimation of elastic modulus by detecting and removing systematic errors. Xu et al. (2009) used the pick-the-winner rule

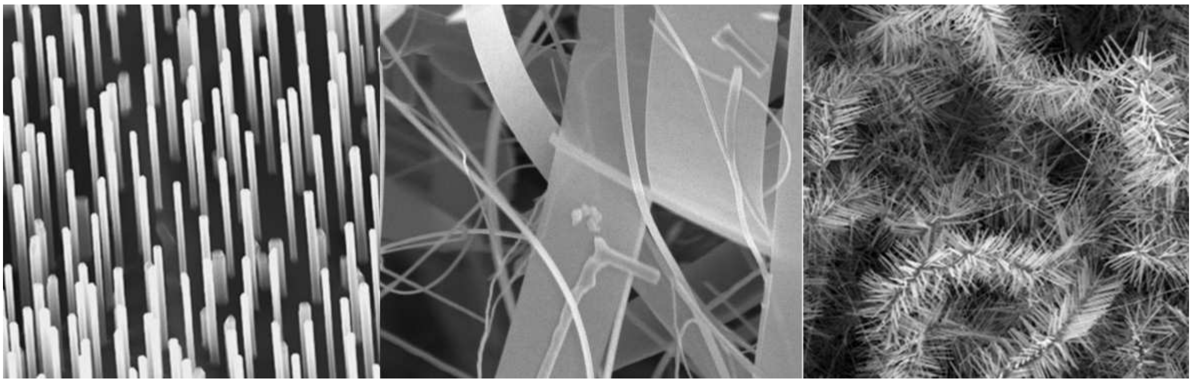


Figure 1: Three types of ZnO nanomaterials: (from left to right) ZnO nanowires, ZnO nanobelts and branched ZnO nanowires.

and one-pair-at-a-time main effect analysis to sequentially design experiments for synthesizing nanomaterials. Mai and Deng (2010) proposed a physical-statistical modeling approach and a global fitting statistical method for quantification of nanomaterials. Song et al. (2010) introduced a statistical model to find the optimal parameter settings for nanomaterials. Wang et al. (2010) developed a statistics-guided approach for accurate characterization of the lengths, diameters, orientations and densities of nanowires. Huang (2011) proposed a Bayesian hierarchical framework for integrating nanosynthesis data and physical knowledge at multiple scales. Huang et al. (2010) provided a modeling approach to describing the overall nanowires growth based on the weight changes during the synthesis process. Dasgupta et al. (2011) proposed a physical-statistical model to enhance the power of predictive models for nanomaterials.

Because nanomaterials have extremely small scales, synthesis experiments for such materials are complex and time-consuming. For illustration, the left panel of Figure 2 presents a sample of a type of zinc-oxide (ZnO) nanowire on a silicon substrate in contrast with a dime. The right panel of the figure shows the scanning electron microscopy image (Wang et al., 2010) of the sample. Each synthesis run of this nanowire takes up to two days to complete. More details of this structure are given in Section 3. ZnO nanowires are known as *two-element* materials in nanotechnology. Three-element compounds, like Barium Titanate

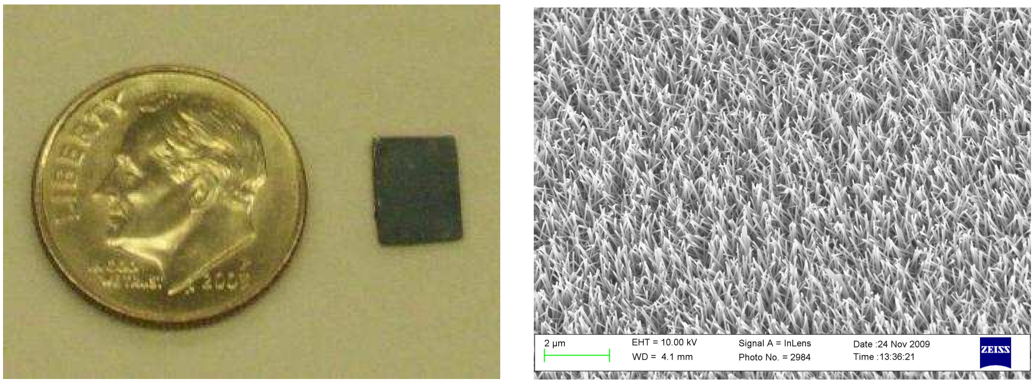


Figure 2: (Left) A sample of ZnO nanowire on a silicon substrate in contrast with a dime; (right) a scanning electron microscopy image of the sample.

($BaTiO_3$), cost even more time to synthesize.

Due to experimental constraints on a single day, scientists in nanotechnology is often confronted with the problem of how to sequentially conduct experiments for synthesizing nanomaterials. A standard approach is to run an initial experiment using a two-level fractional factorial design (Box et al., 2005; Wu and Hamada, 2009) and then conduct a follow-up experiment at a later time by using the fold-over technique (Box and Hunter, 1961) to achieve dealiasing. The augmented design given by this method is still a two-level design. In practice, after an initial nanosynthesis experiment, the experimenter may reckon that some factors may have nonlinear effects, in addition to the need of deliasing the ambiguity among the effects. Section 3 reports a study, where after the initial experiment, in addition to the need of dealiasing, one factor, called PEI concentration, is believed to have possible nonlinear effects. We propose a new statistical design augmentation method, called *level-expansion*, intended for conducting sequential experiments for this situation. For an initial design with two levels, level-expansion constructs a follow-up design by expanding some factors to four elaborately chosen levels and reversing the signs of the remaining factors. The augmented design produced as such strikes a fine balance between dealiasing and entertaining nonlinear effects. In contrast, the augmented design given by fold-over has two levels and can only entertain linear effects. The level-expansion method is general and applies broadly to problems in biology, marketing (Ledolter and Swersey, 2007), the social sciences (Murphy and Bingham, 2009), chemometrics (Phoa et al., 2009a), toxicology (Phoa et al., 2009b), information technology (Yu, 2007; Hung et al., 2010; Hung, 2011) and other fields where a follow-up design is needed for the dual purposes of entertaining nonlinear effects and dealiasing.

The remainder of the article will unfold as follows. Section 2 gives a formal definition of level-expansion and derives its statistical properties, where a simulation example is provided to demonstrate the advantage of level-expansion over fold-over for situations with nonlinear effects. Section 3 further illustrates the effectiveness of the proposed method with a real example for synthesizing a new type of ZnO nanowire. Section 4 provides some discussion.

2 METHODOLOGY

We first give a brief introduction of fractional factorial designs following Wu and Hamada (2009). Let 2^m denote a *full factorial design* at two levels, which consists of all level combinations of m factors (Box et al., 2005; Wu and Hamada, 2009). As m increases, the run size of a 2^m becomes prohibitively large; for example, a 2^8 design would require 256 runs. In view of this drawback, fractional factorial designs were introduced to achieve run size economy. Let 2^{m-p} denote a *fractional factorial design* at two levels in m factors, which is a 2^{-p} fraction of a 2^m design. For illustration, Table 1 gives a 2^{6-3} design, d_1, with eight runs in six factors, A, B, C, D, E and F, which is one eighth of a 2^6 design. Since the column for E equals the product of the columns for A, B and C, the main effect of E is *alised* with the three-factor interaction ABC, denoted by

$$E = ABC \quad \text{or} \quad I = ABCE, \tag{1}$$

where I denotes the column of all +1's. Effect aliasing is a price one must pay for using a fractional factorial design. In (1), $I = ABCE$ is the *defining relation* of the design d_1 and $ABCE$ is its defining word. The number of letters in a defining word is called the wordlength. In general, a 2^{m-p} design is determined by p defining words, which form an algebraic structure called the *defining contrast subgroup* with $2^p - 1$ elements plus the identity element I. The *resolution* of a 2^{m-p} fractional factorial design is the smallest wordlength of the words in the defining contrast subgroup.

Example 1. *The design* d_1 *in Table 1 is determined by the following defining relation:* $I = -ABD$, $I = ABCE$ *and* $I = -BCF$. *The defining contrast subgroup has four words of odd length and three words of even length given by* $I = -ABD = -BCF = -CDE = -AEF = BDEF = ABCE = ACDF$. *As the smallest wordlength of the words in this subgroup is three,* d_1 *has resolution* III. *Any main effect in* d_1 *is aliased with at least one two-factor interaction.*

The *effect sparsity principle* (Wu and Hamada, 2009) stipulates that the number of important effects in an experiment can be small. For example, a 2^8 design requires 256 runs, which can estimate eight main effects and 28 two-factor interactions, with 219 degrees of freedom devoted to entertaining three-factor or higher order interactions. This design can be inefficient when many of the high order interactions are insignificant. A fractional factorial design 2^{8-2} only requires 64 runs and can be a better choice for the same eight factors.

Results of a two-level fractional factorial design can be inconclusive because of the aliasing among the effects. Fold-over (Box and Hunter, 1961) is a popular technique for constructing a follow-up design to resolve such an ambiguity. For a fractional factorial design d at two levels, fold-over creates a follow-up design d^* by reversing the signs of all the factors. That is,

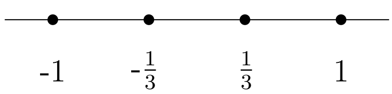
$$d^* = -d. \tag{2}$$

The augmented design of d and d^* has two levels and cannot incorporate any nonlinear effects. In contrast, the level-expansion technique to be constructed in (3) creates a follow-up design that, in conjunction with the initial design d, can entertain some nonlinear effects, in addition to achieving dealising.

Let d_1 be an n by m fractional factorial design with levels -1 and 1. After the completion of an experiment using d_1, suppose that the experimenter now believes k of the m factors can have some nonlinear effects, in addition to being interested in dealiasing. Given this information, the experimenter can use the level-expansion technique to obtain a follow-up design, d_2, by changing the levels $1, -1$ of the k factors with possible nonlinear effects in d to $-1/3$ and $1/3$, respectively, and switch the signs of the remaining $m-k$ factors in d. The design d_2 has the following form:

$$d_2 = \begin{pmatrix} -\frac{1}{3}d_{11} & -d_{12} \end{pmatrix}, \tag{3}$$

where d_{11} consists of the k *expanded* factors and d_{12} consists of the $m-k$ *reversed* factors. For each of the expanded factors in d_2, the signs of the levels are switched and in the meantime the new levels are elaborately chosen to be $-1/3$ and $1/3$ so that after augmenting d_2 to d_1, the factor has four equally spaced levels as displayed below:



For comparison, fold-over creates a follow-up design, d_3, by reversing the signs of all the factors in d_1, where

$$d_3 = \begin{pmatrix} -d_{11} & -d_{12} \end{pmatrix}. \tag{4}$$

In many practical situations like the one described in Section 3, the number of factors to be expanded can be small. Decision on expanding which factors can be made flexibly. One possibility is to choose among the factors in d_1 that have significant main effects. As illustrated in Section 3, subject matter knowledge is also critical to selecting the expanded factors.

Example 2. *Table 2 presents the follow-up designs d_2 and d_3 for d_1 in Example 1. In constructing d_2, the levels of A of d_1 are expanded from -1 and 1 to four levels, -1, $-1/3$, $1/3$ and 1, whereas in constructing of d_3, the levels $1, -1$ of each factor of d_1 are switched to $-1, 1$.*

Let d_L be the augmented design of d_1 and d_2 and let d_F be the augmented design of d_1 and d_3, where the subscripts L and F indicate level-expansion and fold-over, respectively. In

A	B	C	D	E	F
-1	-1	-1	-1	-1	-1
1	-1	-1	1	1	-1
-1	1	-1	1	1	1
1	1	-1	-1	-1	1
-1	-1	1	-1	1	1
1	-1	1	1	-1	1
-1	1	1	1	-1	-1
1	1	1	-1	1	-1

Table 1: A fractional factorial design d_1 with resolution III in six factors with eight runs

d_2						d_3					
A	B	C	D	E	F	A	B	C	D	E	F
1/3	1	1	1	1	1	1	1	1	1	1	1
-1/3	1	1	-1	-1	1	-1	1	1	-1	-1	1
1/3	-1	1	-1	-1	-1	1	-1	1	-1	-1	-1
-1/3	-1	1	1	1	-1	-1	-1	1	1	1	-1
1/3	1	-1	-1	-1	-1	1	1	-1	-1	-1	-1
-1/3	1	-1	1	1	-1	-1	1	-1	1	1	-1
1/3	-1	-1	1	1	1	1	-1	-1	1	1	1
-1/3	-1	-1	-1	-1	1	-1	-1	-1	-1	-1	1

Table 2: A vis-à-vis comparison of the fold-over follow-up design d_2 and the level-expansion follow-up design d_3

addition to estimating linear effects, d_L can entertain some nonlinear effects for the expanded factors. By contrast, d_F is a two-level design and cannot accommodate any nonlinear effect.

Two different decomposition methods from Wu and Hamada (2009) can be used to entertain the four levels of the expanded factors in d_L. The first is to decompose the three degrees of freedom of an expanded factor, say A, via the *linear*, *quadratic* and *cubic* contrasts:

$$\begin{aligned} A_l &= \frac{1}{\sqrt{20}}(\;-3,\;\; -1,\;\; 1,\;\; 3), \\ A_q &= \frac{1}{2}(\;1,\;\; -1,\;\; -1,\;\; 1), \\ A_c &= \frac{1}{\sqrt{20}}(\;-1,\;\; 3,\;\; -3,\;\; 1), \end{aligned} \tag{5}$$

where -3, -1, 1 and 3 in A_l are the weights assigned to observations at levels -1, $-1/3$, $1/3$ and 1, respectively. The weights in A_q and A_c are defined similarly. These contrasts are mutually orthogonal. Hereinafter, the main effects associated with them are called the linear, quadratic and cubic effects, respectively.

Another decomposition system is to replace A_l, A_q and A_c in (5) by

$$\begin{aligned} A_1 &= (\ -1,\ \ -1,\ \ 1,\ \ 1), \\ A_2 &= (\ 1,\ \ -1,\ \ -1,\ \ 1), \\ A_3 &= (\ -1,\ \ 1,\ \ -1,\ \ 1). \end{aligned} \tag{6}$$

These contrasts are still mutually orthogonal and correspond to the *first*, *second* and *third* main effects of A.

Definition 1 describes a linear model that is useful for deriving the aliasing pattern for the augmented design d_L produced by level-expansion.

Definition 1. *Let P be a linear model consisting of the main effects and two-factor interaction effects for all the factors in d_L, where the effects of the expanded factors are defined by (5) or (6). Let $\mathbf{X} = (\mathbf{X}_1, \mathbf{X}_2)$ denote the model matrix of P, with $\mathbf{X}_1$ corresponding to the main effects and $\mathbf{X}_2$ the grand mean and two-factor interactions.*

The alias structure for a model is often defined in terms of an alias matrix (Wu and Hamada, 2009). The alias matrix of P defined in Definition 1 is

$$\mathbf{L} \ = \ (\mathbf{X}_1'\mathbf{X}_1)^{-1}\mathbf{X}_1'\mathbf{X}_2. \tag{7}$$

Here, a main effect in P is said to be *clear* if its corresponding row in $\mathbf{L}$ contains only zero.

Example 3. *Expand factor A of d_1 in Table 1 to obtain d_2, and let d_L to be the combined design of d_1 and d_2. Table 3 gives the alias matrix $\mathbf{L}$ (in transpose) for the model P in Definition 1 with (5) defining the three main effects, A_l, A_q and A_c, of A. Since the columns for A_q and C in Table 3 have only zero, these effects are clear. Table 4 presents the alias matrix $\mathbf{L}$ (in transpose) for the same model but with (6) defining the three main effects, A_1, A_2 and A_3, of A. Since the columns for A_1, A_2 and C in Table 4 have only zero, these effects* *are clear. Note that some columns in Tables 3 and 4 have non-zero entries, suggesting* **L** *is partially aliased.*

	A_l	A_q	A_c	B	C	D	E	F
I	0	0	0	0	0	0	0	0
BC	0	0	0	0	0	0	0	0
BD	-0.894	0	-1.788	0	0	0	0	0
BE	0	0	0	0	0	0	0	0
BF	0	0	0	0	0	0	0	0
CD	0	0	0	0	0	0	0	0
CE	0	0	0	0	0	0	0	0
CF	0	0	0	0	0	0	0	0
DE	0	0	0	0	0	0	0	0
DF	0	0	0	0	0	0	0	0
EF	-0.894	0	-1.788	0	0	0	0	0
A_lB	0	0	0	0	0	-0.223	0	0
A_lC	0	0	0	0	0	0	0	0
A_lD	0	0	0	-0.223	0	0	0	0
A_lE	0	0	0	0	0	0	0	-0.223
A_lF	0	0	0	0	0	0	-0.223	0
A_qB	0	0	0	0	0	0	0	0
A_qC	0	0	0	0	0	0	0	0
A_qD	0	0	0	0	0	0	0	0
A_qE	0	0	0	0	0	0	0	0
A_qF	0	0	0	0	0	0	0	0
A_cB	0	0	0	0	0	-0.447	0	0
A_cC	0	0	0	0	0	0	0	0
A_cD	0	0	0	-0.447	0	0	0	0
A_cE	0	0	0	0	0	0	0	-0.447
A_cF	0	0	0	0	0	0	-0.447	0

Table 3: The alias matrix **L** (in transpose) of the model P in Definition 1 for d_L in Example 3, where the effects of A are defined by (5)

For Example 3, note that the augmented design given by level-expansion can not only dealiase the ambiguity between the main effect of C and the two-factor interactions but also entertain some nonlinear effects of A. To explore this observation more generally, we now derive statistical properties of d_L. As in Bingham et al. (2009), define the J*-characteristic* of n vectors of p entries, $\mathbf{b}_1 = (b_{11}, \ldots, b_{p1})', \ldots, \mathbf{b}_n = (b_{1n}, \ldots, b_{pn})'$, to be

$$J(\mathbf{b}_1, \ldots, \mathbf{b}_n) \;=\; \sum_{i=1}^{p} b_{i1} \ldots b_{in}. \tag{8}$$

	A_1	A_2	A_3	B	C	D	E	F
I	0	0	0	0	0	0	0	0
BC	0	0	0	0	0	0	0	0
BD	0	0	1	0	0	0	0	0
BE	0	0	0	0	0	0	0	0
BF	0	0	0	0	0	0	0	0
CD	0	0	0	0	0	0	0	0
CE	0	0	0	0	0	0	0	0
CF	0	0	0	0	0	0	0	0
DE	0	0	0	0	0	0	0	0
DF	0	0	0	0	0	0	0	0
EF	0	0	1	0	0	0	0	0
A_1B	0	0	0	0	0	0	0	0
A_1C	0	0	0	0	0	0	0	0
A_1D	0	0	0	0	0	0	0	0
A_1E	0	0	0	0	0	0	0	0
A_1F	0	0	0	0	0	0	0	0
A_2B	0	0	0	0	0	1	0	0
A_2C	0	0	0	0	0	0	0	0
A_2D	0	0	0	1	0	0	0	0
A_2E	0	0	0	0	0	0	0	1
A_2F	0	0	0	0	0	0	1	0
A_3B	0	0	0	0	0	0	0	0
A_3C	0	0	0	0	0	0	0	0
A_3D	0	0	0	0	0	0	0	0
A_3E	0	0	0	0	0	0	0	0
A_3F	0	0	0	0	0	0	0	0

Table 4: The alias matrix $\mathbf{L}$ (in transpose) of the model P in Definition 1 for d_L in Example 3, where the effects of A are defined by (6)

Proposition 1 captures the aliasing structure of the model P for d_L using the contrasts in (5).

Proposition 1. *Let d_1 be a fractional factorial design at two levels with resolution III, let d_2 be defined in (3) and let d_L be the augmented design of d_1 and d_2. For the model P of d_L in Definition 1, with the effects of the expanded factors decomposed by (5), we have that*

(i) for any expanded factor, its linear and cubic effects are clear if and only if this factor does not appear in any defining word of d_1 with length three;

(ii) the quadratic effect of any expanded factor is not aliased with any other types of effects;

(iii) the main effect of any reversed factor is clear if and only if this factor does not appear

in any defining word of d_1 that has length three and contains at least one expanded factor.

Proof. For a factor, say A, in d_L, let ζ_A denote its column in d_1. Let $\mathbf{X}$ be the model matrix given in Definition 1, where ξ_a denotes the column for an effect a. For an expanded factor E, let E_l, E_q and E_c denote the linear, quadratic and cubic effects given in (5). Observe that

$$\begin{aligned}
\xi_{E_l} &= \left(\frac{3}{\sqrt{20}}\zeta_E', -\frac{1}{\sqrt{20}}\zeta_E'\right)', \\
\xi_{E_q} &= \left(\frac{1}{2}\mathbf{1}_n', -\frac{1}{2}\mathbf{1}_n'\right)', \\
\xi_{E_c} &= \left(\frac{1}{\sqrt{20}}\zeta_E', \frac{3}{\sqrt{20}}\zeta_E'\right)',
\end{aligned} \tag{9}$$

where $\mathbf{1}_n$ is the nth unit vector. For a reversed factor R in d_L, observe that

$$\xi_R = \left(\ \zeta_R', -\zeta_R'\ \right)'.$$

For (i), only the necessity part needs a proof. Let E be an expanded factor in d_L that does not appear in any defining word of d_1 with length three. For two factors in d_L, say A and B, note that $J(\zeta_E, \zeta_A, \zeta_B) = 0$. To show the main effects E_l and E_c are clear, it suffices to verify that neither E_l nor E_c is aliased with any interaction effect between A and B. For any main effect a of A and any main effect b of B, both $J(\xi_{E_l}, \xi_a, \xi_b)$ and $J(\xi_{E_c}, \xi_a, \xi_b)$ are multiples of $J(\zeta_E, \zeta_A, \zeta_B)$ and thus equal 0.

We now show (ii). For any expanded factor E and two other factors A and B in d_L, it suffices to prove that E_q is not aliased with any two-factor interaction effect between A and B. For any main effect a of A and any main effect b of B, $J(\xi_{E_q}, \xi_a, \xi_b)$ is a multiple of $J(\mathbf{1}_n, \zeta_A, \zeta_B)$, which, because $J(\zeta_A, \zeta_B) = 0$, equals 0. This proves (ii).

For (iii), only the necessity part needs a proof. Let R be a reversed factor that does not appear in any defining word of d_1 with length three containing at least one expanded factor. The proof of (i) implies that the main effect of R is not aliased with any two-factor interaction effect involving an expanded factor. The main effect of R is not aliased with any two-factor interaction effect between two reversed factors because their signs are reversed in d_2. Thus, R is clear, which completes the proof. □

Proposition 2 gives a result for the aliasing structure of the model P for d_L using the contrasts in (6) for the expanded factors.

Proposition 2. *Let d_L be as defined in Proposition 1. For the model P of d_L in Definition 1, with the effects of the expanded factors defined by the contrasts in (6), we have that*

(i) for any expanded factor, its first main effect is clear if and only if this factor does not appear in any defining word of d_1 that has length three and contains more than one expanded factor, and its third main effect is clear if and only if this factor does not appear in any defining word of d_1 with length three;

(ii) the second main effect of any expanded factor is not aliased with any other effect rather than the second main effects;

(iii) the main effect of any reversed factor is clear if and only if this factor does not appear in any defining word of d_1 that has length three and contains at least one expanded factor.

Proposition 2 can be shown by using an argument similar to the proof for Proposition 1 and is thus omitted.

We now illustrate Propositions 1 and 2 in the context of Example 3. The alias matrix $\mathbf{L}$ in Table 3 indicates that if the expanded factor A is decomposed by (5), A_q and the main effect of C are clear. This result follows readily from Proposition 1. As A_q is a quadratic effect, it is clear. As C does not appear in any defining word of d_1 with length three, its main effect is clear. When the contrasts in (6) are used to decompose A, the alias matrix $\mathbf{L}$ in Table 4 indicates that A_1, A_2 and C are clear. This result follows readily from Proposition 2. As A_2 is the second effect of A, it is clear. As A does not appear in any defining word of d_1 that has length three and contains more than one expanded factors, A_1 is clear. Because C

does not appear in any defining word of d_1 that has length three and contains an expanded factor, its main effect is clear.

Because level-expansion can not only deliase but also entertain some nonlinear effects, it is expected to outperform fold-over for situations with significant quadratic or cubic effects. Example 4 illustrates this advantage using a simulation.

Example 4. *Suppose the underlying model of a problem is*

$$y = (x_1 - 0.5)^2 + (x_2 - 0.4)^2 + (x_3 - 0.3)^2 + (x_4 - 0.6)^2 + (x_5 - 0.7)^2 + (x_6 - 0.8)^2 + \epsilon,$$

where $\epsilon \sim N(0, 0.25^2)$. *Without access to this true model, one conducts an experiment using a fractional factorial design* d_1 *with eight runs in Table 1. The six factors in* d_1 *are* A, B, C, D, E *and* F. *Table 5 presents the eight runs and response values. A linear model with the main effects of all factors is fitted to the data from Table 5, with the results given in Table 6.*

Run #	A	B	C	D	E	F	Response
1	-1	-1	-1	-1	-1	-1	15.07
2	1	-1	-1	1	1	-1	7.32
3	-1	1	-1	1	1	1	4.87
4	1	1	-1	-1	-1	1	8.14
5	-1	-1	1	-1	1	1	7.32
6	1	-1	1	1	-1	1	5.91
7	-1	1	1	1	-1	-1	9.14
8	1	1	1	-1	1	-1	7.03

Table 5: Design matrix and responses of a 2^{6-3}_{III} fractional factorial design d_1 for Example 4

Suppose the experimenter now believes that some of the six factors can have nonlinear effects on the response, in addition to being interested in dealiasing. Given this information, a follow-up experiment with eight new runs is conducted in four different ways:

Method I: *Use* d_2 *in (3) constructed by expanding the most significant factor* F *in the initial experiment.*

	Estimate	SE	t value	p-value
A	-1.000	0.120	-8.333	0.07603
B	-0.805	0.120	-6.708	0.09421
C	-0.750	0.120	-6.250	0.10100
D	-1.290	0.120	-10.750	0.05905
E	-1.465	0.120	-12.208	0.05203
F	-1.540	0.120	-12.833	0.04951

Table 6: The fitted linear model consisting of the main effects of all the factors using data from Table 5

Method II: *Use d_2 in (3) constructed by expanding the two most significant factors E and F in the initial experiment.*

Method III: *Use d_2 in (3) constructed by expanding all the six factors of the initial experiment.*

Method IV: *Use d_3 in (4) constructed by fold-over.*

Tables 7-10 present the design matrices and responses produced by these four methods, respectively.

Run #	A	B	C	D	E	F	Response
9	1	1	1	1	1	1/3	1.60
10	-1	1	1	-1	-1	1/3	8.88
11	1	-1	1	-1	-1	-1/3	9.57
12	-1	-1	1	1	1	-1/3	6.38
13	1	1	-1	1	-1	-1/3	6.51
14	-1	1	-1	-1	1	-1/3	8.59
15	1	-1	-1	-1	1	1/3	6.86
16	-1	-1	-1	1	-1	1/3	8.92

Table 7: Design matrix and responses of the follow-up design obtained by Method I

For all the four schemes, the linear model P in Definition 1, consisting of the main effects and two-factor interaction effects of all factors, is fitted to data of the combined design of 16 runs, with the effects of the expanded factors defined by (5). The fitted model is simplified by using (a) the backward selection *procedure based on the* Bayesian Information Criterion *(BIC) (Schwarz, 1978) to select the best model among all main-effect models and (b) the*

Run #	A	B	C	D	E	F	Response
9	1	1	1	1	1/3	1/3	1.295
10	-1	1	1	-1	-1/3	1/3	6.942
11	1	-1	1	-1	-1/3	-1/3	7.746
12	-1	-1	1	1	1/3	-1/3	6.255
13	1	1	-1	1	-1/3	-1/3	4.833
14	-1	1	-1	-1	1/3	-1/3	8.022
15	1	-1	-1	-1	1/3	1/3	6.766
16	-1	-1	-1	1	-1/3	1/3	7.221

Table 8: Design matrix and responses of the follow-up design obtained by Method II

Run #	A	B	C	D	E	F	Response
9	1/3	1/3	1/3	1/3	1/3	1/3	0.774
10	-1/3	1/3	1/3	-1/3	-1/3	1/3	2.771
11	1/3	-1/3	1/3	-1/3	-1/3	-1/3	3.454
12	-1/3	-1/3	1/3	1/3	1/3	-1/3	2.641
13	1/3	1/3	-1/3	1/3	-1/3	-1/3	2.956
14	-1/3	1/3	-1/3	-1/3	1/3	-1/3	3.547
15	1/3	-1/3	-1/3	-1/3	1/3	1/3	2.143
16	-1/3	-1/3	-1/3	1/3	-1/3	1/3	3.407

Table 9: Design matrix and responses of the follow-up design obtained by Method III

Run #	A	B	C	D	E	F	Response
9	1	1	1	1	1	1	1.21
10	-1	1	1	-1	-1	1	8.77
11	1	-1	1	-1	-1	-1	11.46
12	-1	-1	1	1	1	-1	8.13
13	1	1	-1	1	-1	-1	8.56
14	-1	1	-1	-1	1	-1	10.41
15	1	-1	-1	-1	1	1	6.50
16	-1	-1	-1	1	-1	1	9.05

Table 10: Design matrix and responses of the follow-up design obtained by Method IV

subset selection procedure that identifies the best model among all candidate models with no more than five effects under the effect heredity *principle (Wu and Hamada, 2009). For each scheme, the mean square error (MSE) for the final model on a set of 5,000 randomly generated points from* $[-1, 1]^6$ *is computed.*

Table 11 presents the models chosen by the backward selection procedure, where the main effects of A*,* B*,* C*,* D*,* E *and* F *appear significant in all the four schemes. Table 12 gives the* *results of the models chosen by the subset selection procedure, where the main effects of A, B, C, D, E and F appear significant in all the four schemes. These tables demonstrate that level-expansion outperforms fold-over in terms of the MSEs. Among the three level-expansion schemes, Method III performs the best, which is not surprising, as all the factors in the true model have significant nonlinear effects.*

Methods	Significant Effects	MSE	R^2	BIC
I	A, B, C, D, E, F_l, F_q	12.08	0.996	12.72
II	A, B, C, D, E_l, F_l, F_q	7.52	0.996	9.46
III	A_l, B_l, C_l, D_l, D_c, E_l, F_l, F_q	2.75	0.998	9.76
IV	A, B, C, D, E, F	17.24	0.997	3.04

Table 11: Significant effects in the final model chosen by the backward selection procedure for Example 4

Methods	Significant Effects	MSE	R^2	BIC
I	B, D, E, F_l, EF_c	14.75	0.881	62.50
II	D, E_l, F_l, F_q, F_lE_c	10.57	0.840	67.14
III	A_l, A_q, E_l, F_l, A_lB_l	3.56	0.935	60.63
IV	A, D, E, F, AC	17.34	0.869	66.37

Table 12: Significant effects in the final model chosen by the subset selection procedure for Example 4

3 CASE STUDY

In this section, the effectiveness of the proposed method is further illustrated with a case study for synthesizing a new type of ZnO nanowire. Figure 3 presents the schematic of the synthesis process, which uses an aqueous solution involving $Zn(NO_3)_2$, hexamethylenetetramine (HMTA) and polyethyleneimine (PEI). As shown in the left panel of Figure 4, in the synthesis process, a silicon wafer is first placed in a reaction vial containing the reaction solution and the vail is then stored in an oven at 70°C-90°C for 24 hours presented in the right panel of the figure.

The nutrient solution is preheated to the growth temperature before loading the sub-

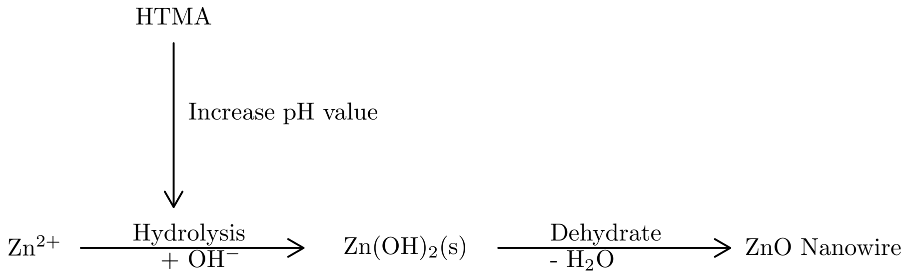


Figure 3: Schematic illustration of the synthesis process of a new type of ZnO nanowire.

Figure 4: (Left) A silicon wafer is placed in a reaction vial containing the reaction solution, where the deposition side with ZnO faces down; (right) the reaction vial is placed in an convection oven.

strates. The response of the study is nanowire length, measured via scanning electron microscope devices (Wang et al., 2010). This study investigates the effects of six factors, concentration of PEI (x_1), growth temperature (x_2), concentration of $ZnNO_3$ (x_3), concentration of Hexamine (x_4), growing time (x_5) and preheat (x_6), on the length of nanowires grown on the substrate. Table 13 presents the factors and their design ranges, where preheat is qualitative and the others are quantitative. The levels of each factor are also coded as -1 and 1. If the factor is quantitative, these coded levels represent the lower and upper bounds

Factors		
x_1: Concentration of PEI	0.0g/L	3.0g/L
x_2: Growth Temperature	70°C	90°C
x_3: Concentration of $Zn(NO_3)_2$	20 mM	50 mM
x_4: Concentration of Hexamine	20 mM	50 mM
x_5: Growing time	4 hours	10 hours
x_6: Preheat	No	Yes

Table 13: Factors and their design ranges in the ZnO nanowire study

of the design range.

3.1 DESIGN AND ANALYSIS OF AN INITIAL EXPERIMENT WITH EIGHT RUNS

An experiment is conducted using a 2^{6-3}_{III} fractional factorial design with generators $4 = -12, 5 = 123$ and $6 = -23$, with one replication per each level combination. The design matrix and responses are given in Table 14. Figure 5 depicts the main effects plots for data from the experiment, where the main effects of x_1, x_5 and x_6 appear significant.

Run #	x_1	x_2	x_3	x_4	x_5	x_6	Response (nm)
1	0	70	20	20	4	No	1.26
2	3	70	20	50	10	No	3.11
3	0	90	20	50	10	Yes	1.27
4	3	90	20	20	4	Yes	0.71
5	0	70	50	20	10	Yes	0.87
6	3	70	50	50	4	Yes	0.63
7	0	90	50	50	4	No	0.90
8	3	90	50	20	10	No	3.35

Table 14: Design matrix and responses for eight initial runs, a 2^{6-3}_{III} design, for the ZnO nanowire study

3.2 A FOLLOW-UP EXPERIMENT VIA LEVEL-EXPANSION

After the initial experiment is completed, background knowledge of this example leads us to suspect that some of the six factors can affect the response in a nonlinear fashion, in addition to the need of dealiasing the ambiguity among the factors. In particular, interest

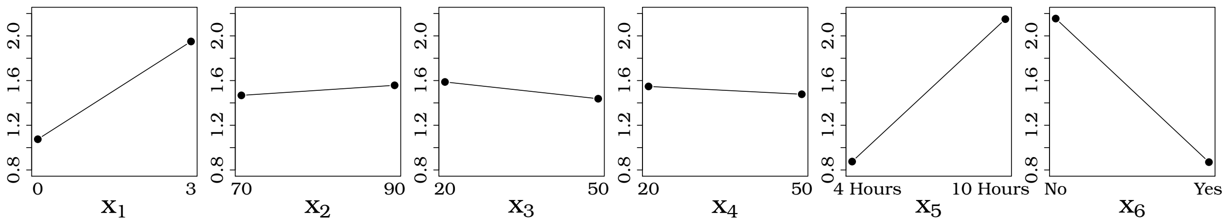


Figure 5: Main effects plots of the six factors for the ZnO nanowire study.

Run #	x_1	x_2	x_3	x_4	x_5	x_6	Response (nm)
9	2	90	50	50	10	Yes	2.06
10	1	90	50	20	4	Yes	1.74
11	2	70	50	20	4	No	0.60
12	1	70	50	50	10	No	1.19
13	2	90	20	50	4	No	1.04
14	1	90	20	20	10	No	2.86
15	2	70	20	20	10	Yes	1.42
16	1	70	20	50	4	Yes	1.14

Table 15: Design matrix and responses for a follow-up experiment with eight runs for the ZnO nanowire study

lies in investigating whether PEI concentration (x_1) has some nonlinear effect on the growth of nanowires. The relationship between this factor and nanowire growth is especially intriguing from a scientific point of view. This relationship has not been thoroughly studied in nantechnolgy prior to the current study and cannot be precisely captured by any existing physical or chemical models. In this light, a decision is made to expand x_1 using the level-expansion technique described in Section 2. Table 15 gives the design matrix and responses for the follow-up design d_2 with eight runs constructed by (3). In the columns for x_1 in Tables 14 and 15, after the design region $[0, 3]$ is scaled to $[-1, 1]$, the four levels, 0, 1, 2 and 3, correspond to -1, $-1/3$, $1/3$ and 1, the same as those in the display below (3). Note that x_1 is one of the three significant factors identified by the initial experiment shown in Figure 5.

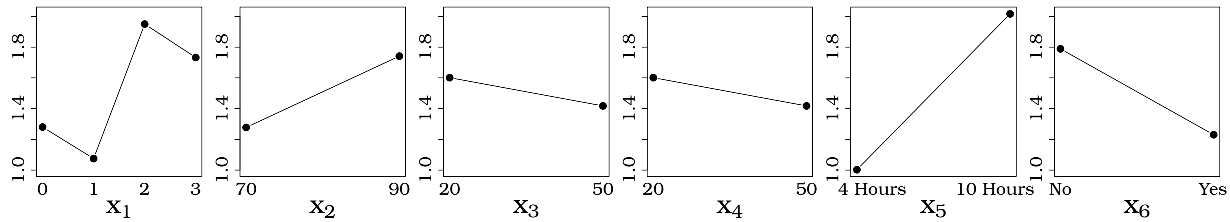


Figure 6: Main effects plots of the six factors based on the combined 16 runs for the ZnO nanowire study.

3.3 INTEGRATED ANALYSIS OF THE INITIAL AND FOLLOW-UP EXPERIMENTS

Figure 6 depicts the main effects plots for all 16 runs from the initial experiment and the follow-up experiment. Among the six factors, x_1 appears to have significant nonlinear effects. This finding confirms our conjecture before the follow-up experiment that this factor can affect the response in a nonlinear fashion. The linear model P given in Definition 1 is fitted to the 16 runs using (5) to decompose the four levels of x_1. Here, the subset selection procedure described in Example 4 is employed to simplify the fitted model.

	Estimate	SE	t value	p-value
(Intercept)	1.5094	0.0827	18.25	0.0000
x_{1c}	-0.4724	0.3698	-1.28	0.2303
x_5	0.5069	0.0827	6.13	0.0001
$x_{1c}x_4$	-0.5819	0.1654	-3.52	0.0055
x_5x_{1l}	0.8995	0.1654	5.44	0.0003
x_5x_6	-0.5431	0.1849	-2.94	0.0148

Table 16: Coefficients of the selected model fitted to the 16 runs for the ZnO nanowire study

Table 16 summarizes the coefficients of the final model fitted to the 16 runs for the ZnO nanowire study. Residual plots for the model do not exhibit any pattern of concern (not shown here), suggesting a decent model fit.

The significant effects in Table 16 include the cubic effect of x_1 and the interaction effect between x_1 and x_4, neither of which would have been detected if the eight follow-up runs in Section 3.2 were obtained by fold-over. The use of the level-expansion method in this example successfully unveils some previously unknown nonlinear relationships in nontechnology. Not only x_1 is found some significant main effect, it also has significant interactions with two other factors. By further exploring these important nonlinear relationships, nanoscientists can produce ZnO nanowires and other one-dimensional nanostructures with better macroscopic transport properties.

4 DISCUSSION

As nanotechnology is rapidly changing the way people work and live, the accelerating development of this area provides ample opportunities for developing new statistical methods. Inspired by a practical problem of sequential synthesis of nanomaterials, we have proposed a new statistical design augmentation method, called level-expansion. This method expands some factors of a two-level fractional factorial design to four elaborately chosen levels and reverses the signs of the other factors in order to simultaneously achieve dealiasing and entertain some nonlinear effects. The effectiveness of the proposed method has been successfully illustrated with a real example of synthesizing a type of ZnO nanowire. The method is easy to implement and does not involve any intensive computing. It needs be stressed here that the proposed method is very general and applies broadly to problems in sciences, engineering, marketing and the social science where a follow-up design is needed for the dual purposes of accommodating nonlinear effects and dealiasing.

Though some headway has been made here to examine statistical properties of level-expansion, much is still unknown about this new method. It is expected this method will attract further research interest in the statistical design and analysis of experiments community and beyond to further explore its theoretical properties and possible extensions.

Selection of the expanded factors in level-expansion can be made very flexibly. One possibility is to choose among the factors in the initial experiment that have significant effects. On the contrary, one may expand some of the factors in the initial experiment that have insignificant main effects but potential nonlinear effects. As demonstrated in Section 3, when the level-expansion technique is applied to solve a practical problem, subject matter information should have the final say on determining which factors to be expanded.

For the ZnO nanawire synthesis experiment in Section 3, -1 and 1 are the design boundaries for the expanded factor and thus the two new levels, $-1/3$ and $1/3$, are taken within the interval of $[-1, 1]$. For other applications, one may choose the new levels outside the design range of the initial experiment. This extrapolating expansion is appealing for investigating new phenomenon beyond conventional design regions, e.g., studying the growth of semiconductor wafers under extreme temperature or humidity conditions.

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