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Experimental Designs for Computer Experiments and for Industrial Experiments with Model Unknown[†]

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ABSTRACT

Most statistical designs, such as orthogonal designs and optimal designs, are based on a specific statistical model. It is very often that the experimenter does not completely know the underlying model between the response and the factors. In computer experiments, the underlying model is known, but too complicated. In this case we can treat the model as a black box, or model to be unknown. Both cases need a space filling design. The uniform design is one of space filling designs and seeks experimental points to be uniformly scattered on the domain. The uniform design can be used for computer experiments and also for industrial experiments when the underlying model is unknown. In this paper we shall introduce the theory and method of the uniform design and related data analysis and modelling methods. Applications of the uniform design to industry and other areas are discussed.

Keywords. Computer experiments, experiment with mixtures, factorial design, uniform design.
AMS 2000 subject classifications. Primary 93B52; Secondary 62K15.

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1. Introduction

Statistical experimental design has a long history and is a powerful tool in various fields. Most experimental design methods concern with randomness, balance, orthogonality, efficiency, and robustness under a specific statistical model. For example, the factorial design is based on a ANOVA model and the optimal design is based on a regression model with some unknown parameters.

Example 1. In a biological experiment we wish to explore the relationship between the growth time (x) and the response (y). The underlying model

$$y = y(x) = 1 - e^{-2x^2}, \quad x \in [0, 2], \tag{1.1}$$

is unknown. Figure 1 gives a plot of the growth curve. There are many ways to design this experiment based on different statistical models. The followings are some of them.

A. ANOVA Models

The experimenter observes the response at several growth times, $x_1, \cdots, x_q$, that are called *levels*. For each x_j we repeat experiment n_j times and related responses are $y_{1j}, \cdots, y_{n_j j}$. A statistical model

$$y_{ij} = \mu_j + \epsilon_{ij}, \quad j = 1, \cdots, q, i = 1, \cdots, n_j, \tag{1.2}$$

where μ_j is the true value $y(x_j)$ and ϵ_{ij} are random errors that are independently identically distributed according to $N(0, \sigma^2)$. Let μ be the overall mean of y over $x_1, \cdots, x_q$. Then the mean μ_j can be decomposed into $\mu_j = \alpha_j + \mu$, where α_j is called the main effect of y at x_j and they satisfy $\alpha_1 + \cdots + \alpha_q = 0$.

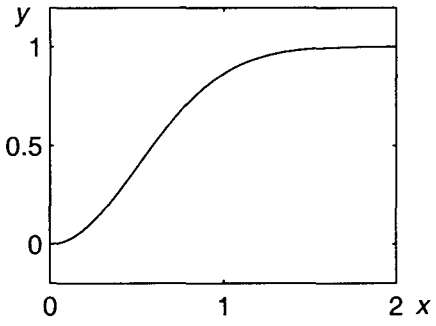
Under model (1.2) we need to find a design under which we can efficiently estimate $\{\mu_1, \cdots, \mu_q\}$ or $\{\mu, \alpha_1, \cdots, \alpha_q\}$ and σ^2, and to assess whether $y(x)$ significantly depends on $x = x_1, \cdots, x_q$. The so-called *factorial designs* can reach this task.

B. Linear regression models

From the professional knowledge the experimenter wants to use a linear model to fit relationship between x and y

$$y(x) = \beta_1 f_1(x) + \cdots + \beta_m f_m(x) + \epsilon, \quad x \in \mathcal{T}, \tag{1.3}$$

where $\mathcal{T}$ is the experimental domain, functions $f_1, \cdots, f_m$ are known and $\beta_1, \cdots, \beta_m$ are unknown. We want to design an experiment with a fixed number of runs



FIGRURE 1 *Weibull growth curve model*

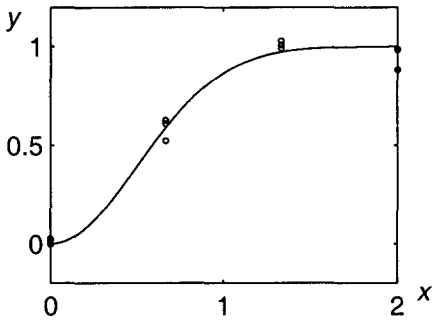


FIGURE 2 *Factorial design*

such that we can obtain the best estimators of $\beta_1, \cdots, \beta_q$ and σ^2. The so-called *optimal design* is from this idea. There are several criteria, such as D-optimality, A-optimality, E-optimality, *etc.* in theory of optimal designs. See Atkinson and Donev (1992) and Pulkelsheim (1993) for the details. When model (1.3) is

$$y(x) = \beta_0 + \beta_1 x + \beta_2 x^2 + \epsilon, \tag{1.4}$$

the corresponding D-optimal design is presented in Figure 3, where the dash line is the fitting curve. We can see that the fitting is not well, as model (1.4) is wrong. So the optimal design does not have robustness against model changes.

C. Nonparametric regression models

When the experimenter do not have any prior knowledge about the underlying model, a nonparametric regression model

$$y = g(x) + \epsilon, \quad \mathbf{x} \in \mathcal{T} \tag{1.5}$$

where function g is unknown, can be employed. We want to estimate $y(x)$ at each x. Many smooth techniques, such as polynomial regression model, kernel estimator, local polynomial fitting, wavelets, spline, *etc.* can be used to estimate the function g. Under model (1.5) the *uniform design* is recommended. A uniform design with 12 runs is shown in Figure 4, where the dash line is the fitting curve by a polynomial regression model.

D. Robust regression models

If the experimenter knows the underlying model to be close to a linear model, a robust regression model is

$$y(x) = \beta_1 f_1(x) + \cdots + \beta_m f_m(x) + h(x) + \epsilon, \quad \mathbf{x} \in \mathcal{T} \tag{1.6}$$

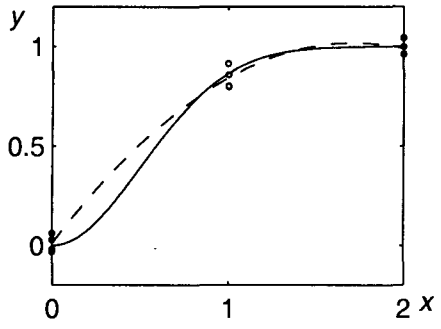


FIGURE 3 *Optimal design*

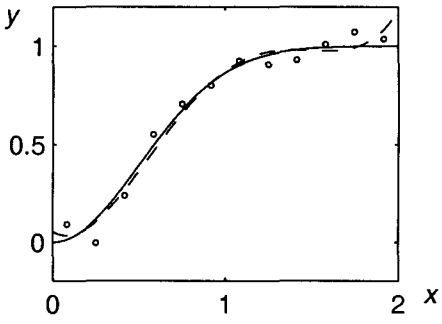


FIGURE 4 *Uniform design*

where $h(x)$ denotes the departure of the model (1.5) from the true model. When function h belongs to some class of functions, we wish to find a design such that we can obtain the best estimators for $\beta_1, \cdots, \beta_m$ under a certain sense. It has shown that the uniform design is a robust design against model changes.

Multi-factor experiments, especially in high-tech development, have the following complexities: (a) many factors; (b) large experimental region; (c) complicated non-linear model; and (d) model unknown. Due to these complexities one needs some new experimental designs. The space filling design is a good alternative choice, especially when the underlying model is unknown.

Design of computer experiments is a rapidly growing area and is particularly useful in the system engineering. It has been paid much attention in the past two decades. Suppose that we have a device/process in a system engineering or in a financial system. The behavior of the device/process depends on a number of input variables $x_1, \cdots, x_s$. Based on the professional knowledge we can calculate the responses from the input variables by

$$y = g(x_1, \cdots, x_s), \ \mathbf{x} = (x_1, \cdots, x_s) \in \mathcal{T}, \tag{1.7}$$

where $\mathcal{T}$ is the input space. Due to complexity and nonlinearity of the device/process the function g has no analytic formula. One wishes to find an approximate model $y = \hat{g}(x_1, \cdots, x_s)$ that is much simpler than the true one based on a set of design points and their responses (*cf.* Figure 5).

If one can find such an approximation model $\hat{g}$, there are many goals that may be requested from the practice. For example,

(a) **Visualization**

The model $\hat{g}$ can serve as a primitive way to visualize the true model g. For example, plots of y against each factor, contour plots of y against each pair of

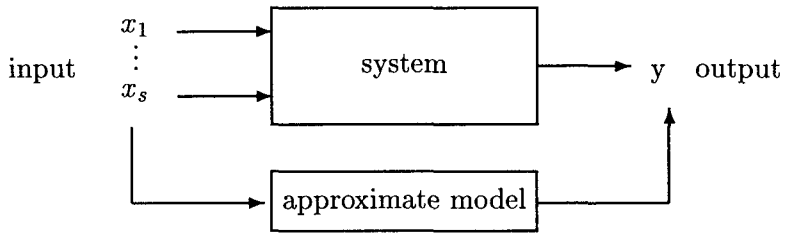


FIGURE 5 *Computer experiments*

the factors, *etc.*

(b) **Optimization**

The experimenter can estimate the minimum/maximum value of the response y and the related minimum/maximum point. The solution can be approximately found by finding a point $\mathbf{x}^* = (x_1^*, \cdots, x_s^*) \in \mathcal{T}$ such that

$$\hat{g}(x_1^*, \cdots, x_s^*) = \min_{\mathbf{x} \in \mathcal{T}} \hat{g}(x_1, \cdots, x_s),$$

if one wishes to find the minimum value of y. The above optimization can be implemented under some constrains. This kind of optimization is often impossible by the use of response surface.

(c) **Estimation**

When the overall mean of y over the region $\mathcal{T}$ is the interest, the true value of the overall mean is given by the integration

$$E(y|\mathcal{T}) = \int_{\mathcal{T}} g(\mathbf{x}) d\mathbf{x}$$

that can be approximated (estimated) by

$$I(g|\mathcal{T}) = \int_{\mathcal{T}} \hat{g}(\mathbf{x}) d\mathbf{x}.$$

In fact, one can estimate many other interesting parameters through the approximation model.

Now, we face *Design and Modeling problems*:

(i) **Construction of uniform designs**: How do we choose a set of experimental points, $\mathcal{P} = \{\mathbf{x}_1, \cdots, \mathbf{x}_n\}$, on the region $\mathcal{T}$ such that these points are uniformly scattered on the region $\mathcal{T}$. We need a measure of uniformity and a powerful algorithm for searching uniform designs.

(ii) **Modelling:** How do we find a good approximation model $\hat{g}$. It needs many techniques in statistical modeling and in curves and surfaces for computer-aided design in engineering (CAD/CAM techniques) (Frarin, 1993).

A comprehensive review on the space filling design can refer to Bates *et al.* (1996) and Koehler and Owen (1996). The uniform design (UD) is one of space filling designs and it seeks experimental points to be uniformly scattered on the domain. The UD was proposed by Fang and Wang (Fang, 1980; Wang and Fang, 1981) and has been popularly used since 1980. A comprehensive studies on the uniform design can refer to Fang and Wang (1994), Fang and Hickernell (1995), Fang *et al.* (2000), and Fang and Lin (2002). The UD has several advantages. For example, it can explore relationships between the response and the factors with a reasonable number of runs and is robust to the underlying model specifications. For practical ease, most uniform designs have been constructed and tabulated for the practitioners.

2. Uniform Designs in Computer and Industrial Experiments

The uniform design for multi-factor experiments can be tabulated. For an experiment of n runs and s factors on the experimental region $\mathcal{T}$, a uniform design for this experiment is to put n points uniformly scattered on $\mathcal{T}$. Very often the experimental region is a rectangle $[\mathbf{a}, \mathbf{b}] = [a_1, b_1] \times \cdots \times [a_s, b_s]$. For the jth factor, suppose one chooses q equi-distance points (we might call then as *levels*), denoted by $x_{j1}, \cdots, x_{jq}$, $q \leq n$ and q is a divisor of n. There are q^s level-combinations. By a linear transformation, these q levels becomes $1, \cdots, q$, called as canonical levels. A uniform design is used for choosing a subset of n points from these q^s level-combinations.

Definition 2.1. *A matrix of $n \times s$ is called a U-type design of $U(n; q^s)$ if each column of the matrix has $1, 2, \cdots, q$ as its elements and these elements appear equally often.*

Definition 2.2. *A uniform design table $U_n(q^s)$ (UD table for short) is a U-type design $U(n; q^s)$ and has the best uniformity (in terms of choice of measure of uniformity) among all such $U(n; q^s)$ designs.*

Therefore, q must be a divisor of n. In Section 4 we shall introduce measures of uniformity and the construction of uniform designs. Table 1 gives a UD table $U_{12}(12^4)$ that can help us to choose 12 runs from 12^4 level-combinations if k

in the jth column of the table $U_n(q^s)$ corresponds to x_{jk} for $j = 1, \cdots, s, k = 1, \cdots, n$. Many uniform design tables can be downloaded from world web site at http://www.math.hkbu.edu.edu.hk/UniformDeisgn (UD-web site for short) .

TABLE 1 *UD table* $U_{12}(12^4)$

No.	**1**	**2**	**3**	**4**
1	1	10	4	7
2	2	5	11	3
3	3	1	7	9
4	4	6	1	5
5	5	11	10	11
6	6	9	8	1
7	7	4	5	12
8	8	2	3	2
9	9	7	12	8
10	10	12	6	4
11	11	8	2	10
12	12	3	9	6

Example 2. A chemical experiment is conducted in order to find the best setup to increase the yield. The following subsections illustrate the procedure of implementing uniform design, step by step.

2.1. Choose factors and their levels

Four factors, the amount of formaldehyde (x_1), the reaction temperature (x_2), the reaction time (x_3), and the amount of potassium carbolic acid (x_4) are under the consideration. The response variable is designated as the yield (y). The experimental domain is chosen to be $\mathcal{T} = [1.0, 5.4] \times [5, 60] \times [1.0, 6.5] \times [15, 70]$ and each factor takes 12 levels as follows:

The amount of formaldehyde (mol/mol): 1.0, 1.4, 1.8, 2.2, 2.6, 3.0, 3.4, 3.8, 4.2, 4.6, 5.0, 5.4
The reaction temperature (hour): 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60
The reaction time (hour): 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5
The amount of potassium carbolic

acid (ml): 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65

The four factors in this example are quantitative. In fact, factors in industrial experiments can be quantitative or qualitative. The uniform design can deal with categorical factors as well.

2.2. Design and run experiments

This experiment could be arranged with a UD table of the form $U_n(12^4)$, where 12 is a divisor of n. It turns out that the experimenter chooses $U_{12}(12^4)$ design in Table 1. The 12 levels marked by $1, 2, \ldots, 12$ are transformed into the real levels of the factors. It results in a design listed in Table 2. Specifically, the heading of (**1, 2, 3, 4**) in Table 2 represents the uniform design table for four factors in twelve runs. The heading of (x_1, x_2, x_3, x_4) in Table 2 represents the actual experimental values for these four factors. Randomize the order of these 12 level-combinations, implement the experiments, and record the corresponding yield y (see the last column of Table 2).

TABLE 2 $U_{12}(12^4)$ *and related design*

No.	**1**	**2**	**3**	**4**	x_1	x_2	x_3	x_4	y
1	1	10	4	7	1.0	50	2.5	45	0.0795
2	2	5	11	3	1.4	25	6.0	25	0.0118
3	3	1	7	9	1.8	5	4.0	55	0.0109
4	4	6	1	5	2.2	30	1.0	35	0.0991
5	5	11	10	11	2.6	55	5.5	65	0.1266
6	6	9	8	1	3.0	45	4.5	15	0.0717
7	7	4	5	12	3.4	20	3.0	70	0.1319
8	8	2	3	2	3.8	10	2.0	20	0.0900
9	9	7	12	8	4.2	35	6.5	50	0.1739
10	10	12	6	4	4.6	60	3.5	30	0.1176
11	11	8	2	10	5.0	40	1.5	60	**0.1836**
12	12	3	9	6	5.4	15	5.0	40	0.1424

2.3. Modelling

The major goal of the data analysis is to establish a suitable approximate model to the true one. We have mentioned that there are many ways to search a such model. In this example, we consider only linear and quadratic regression

models.

Note that the goal of the experiment is to find the best level-combination of the factors that can maximize the yield. The best result among the 12 responses is $y_1 = 18.36\%$ at $x_1 = 5.0, x_2 = 40$, $x_3 = 1.5$ and $x_4 = 60$. This can be served as a benchmark. We wish to know whether there is any level-combination to produce a better yield. The simplest approximate model is the first-order regression:

$$E(y) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4.$$

Based on the data in Table 2, we get model

$$\hat{y} = -0.0533 + 0.0281 x_1 + 0.0010 x_2 - 0.0035 x_3 + 0.0011 x_4.$$

In the ANOVA table, the model involves an insignificant term 'x_3' with p-value 0.4962. We have to remove this term from the model. By the backward elimination techniques in regression analysis, the resulting model turns out to be

$$\hat{y} = 0.0107 + 0.0289 x_1$$

with $R^2 = 57.68\%$ and $s^2 = 0.0014$. This model is not consistent with experience of the experimenter as there are three factors not to be involved in the model. Therefore, a more flexible second-order quadratic regression is considered,

$$E(y) = \beta_0 + \sum_{i=1}^{4} \beta_i x_i + \sum_{i \le j} \beta_{ij} x_i x_j.$$

With MAXR, a technique of selection of variables, we find

$$\begin{aligned} \hat{y} = \; & 0.0446 + 0.0029 x_2 - 0.0260 x_3 + 0.0071 x_1 x_3 \\ & + 0.000036 x_2 x_4 - 0.000054 x_2^2 \end{aligned} \tag{2.1}$$

with $R^2 = 97.43\%$ and $s^2 = 0.0001$. Statistical diagnostics based on the residual and normal plots indicate that the model (2.1) is acceptable.

In the literature, the centered second-order centered quadratic regression model

$$E(y) = \beta_0 + \sum_{i=1}^{4} \beta_i (x_i - \bar{x}_i) + \sum_{i \le j} \beta_{ij} (x_i - \bar{x}_i)(x_j - \bar{x}_j)$$

is recommended, where $\bar{x}_i$ is the sample mean of x_i. In this data set, $\bar{x}_1 = 3.2$, $\bar{x}_2 = 32.5$, $\bar{x}_3 = 3.75$ and $\bar{x}_4 = 42.5$. Once again, by using model selection techniques, the final model is

$$\begin{aligned}\hat{y} = \; & 0.1277 + 0.0281(x_1 - 3.2) + 0.000937(x_2 - 32.5) \\ & +0.00114(x_4 - 42.5) + 0.00058(x_3 - 3.75)(x_4 - 42.5) \\ & -0.000082(x_2 - 32.5)^2 \end{aligned} \tag{2.2}$$

with $R^2 = 97.05\%$ and $s^2 = 0.0002$. The residual plot and normal plot are shown that the model (2.2) is acceptable.

2.4. Prediction and optimization

Models (2.1) and (2.2) obtained in the previous step can be used to predict response at any point of the experimental domain. It also can be used for searching the 'best' combination of the factor-value. We maximize y with respect to $x_i, i = 1, \ldots, 4$ under Models (2.1) or (2.2) respectively over the domain $\mathcal{T}$ given in *Step 1*, that is to find $x_i^*, i = 1, \ldots, 4$ such that

$$\hat{y}(x_1^*, x_2^*, x_3^*, x_4^*) = \max_{\mathcal{T}} \hat{y}(x_1, x_2, x_3, x_4),$$

where $\hat{y}(x_1, x_2, x_3, x_4)$ is given by (2.1) or (2.2) respectively. By any optimization algorithm, it is easily found that under Model (2.1), the maximum point is $x_1^* = 5.4$, $x_2^* = 50.2$, $x_3^* = 1$, $x_4^* = 70$ with $\hat{y}(5.4, 50.2, 1, 70) = 19.3\%$; and under Model (2.2), the maximum point is $x_1^* = 5.4$, $x_2^* = 43.9$, $x_3^* = 6.5$, $x_4^* = 70$ with the maximum response $\hat{y}(5.4, 43.9, 6.5, 70) = 26.5\%$. It looks Model (2.2) to be better, but we need some additional experiment to judge this guess and to see which model is closer to the real one.

2.5. Additional experiments

As two optimal points $\mathbf{x}_1^* = (5.4, 50.2, 1, 70)$ and $\mathbf{x}_2^* = (5.4, 43.9, 6.5, 70)$ do not appear in the plan (Table 2), some additional experiments are necessary. A simplest way is to implement m runs at these two optimal points $\mathbf{x}_1^*$ and $\mathbf{x}_2^*$ and to compare their mean yield. Alternatively, the experimenter should consider a further investigation and arrange a consequent experiment, for instance, one can consider another uniform design on the domain that can cover $\mathbf{x}_1^*$ and $\mathbf{x}_2^*$ and can increase upper bound of the experimental level for x_1 and x_4.

2.6. Remarks

From the above demo example we can see that the uniform design is suitable for the case where the underlying model is unknown. There are two major parts: *design and modelling.* In the design part we borrow the concept of level from the factorial design to choose a set of points uniformly scattered on the experimental domain. For the modelling part the literature provides many smoothing techniques, such as (orthogonal) polynomial regression, multivariate spline (Stone, Hansen, Kooperberg and Truong, 1997), wavelets (Chui, 1992; Antouiadis and Oppenheim, 1995), neural network (Caudill and Butler, 1992), and slice inverse regression (SIR)(Li, 1991). It has no space to introduce all these methods, the reader can refer to the references for the details.

For computer experiments in a system, the output of y can be determined by (1.7). Due to complexity of the model, one wishes to find an approximation model to the true one (1.7)

$$y = \hat{g}(x_1, \cdots, x_s), \quad \mathbf{x} = (x_1, \cdots, x_s) \in \mathcal{T}, \tag{2.3}$$

that has an analytic expression and is simpler than the true one. The uniform design can choose a set of points on $\mathcal{T}$ based on which we could find a suitable approximation model $\hat{g}(x_1, \cdots, x_s)$. Obviously, the above discussion on design and modelling techniques can be applied to computer experiments. For industrial experiments the number of runs is small for most cases due to limited budget while for computer experiments the number of runs can be much larger. The reader can refer to Fang *et al.* (2000), Li (2002), and Fang and Lin (2002) for some interesting examples.

3. Measures of Uniformity and Construction of Uniform Designs

Let $\mathcal{P} = \{\mathbf{x}_1, \cdots, \mathbf{x}_n\}$ be a set of experimental points on the unit cube $C^s = [0, 1]^s$. There are many measures of uniformity, such as the star discrepancy, star L_2-discrepancy, centered L_2-discrepancy (CD) and wrap-around L_2-discrepancy (WD) (see Niederreiter, 1992; Hickernell, 1998). The last two measures have good properties for construction of uniform designs and are easily to compute. A computational formula for these two measures are given by

$$(CD_2(\mathcal{P}))^2 = \left(\frac{13}{12}\right)^s - \frac{2}{n}\sum_{k=1}^{n}\prod_{j=1}^{s}\left(1+\frac{|x_{kj}-0.5|}{2}-\frac{|x_{kj}-0.5|^2}{2}\right)$$
$$+\frac{1}{n^2}\sum_{k=1}^{n}\sum_{j=1}^{n}\prod_{i=1}^{s}\left[1+\frac{|x_{ki}-0.5|}{2}+\frac{|x_{ji}-0.5|}{2}-\frac{|x_{ki}-x_{ji}|}{2}\right] \quad (3.1)$$

and

$$(WD_2(\mathcal{P}))^2 = \left(\frac{4}{3}\right)^s + \frac{1}{n^2}\sum_{k=1}^{n}\sum_{j=1}^{n}\prod_{i=1}^{s}\left[\frac{3}{2}-|x_{ki}-x_{ji}|(1-|x_{ki}-x_{ji}|)\right], \quad (3.2)$$

where $\mathbf{x}_k = (x_{k1}, \cdots, x_{ks})$.

Suppose we wish to find a uniform design $U_n(q^s)$(*cf.* Definition 2.2) for a given measure of uniformity, for example the centered L_2-discrepancy CD. We need to find a U-type design $U(n; q^s)$ such that it has the smallest CD-value among all $U(n; q^s)$ designs. This is an optimization problem and is a NP hard problem in terms of complexity of the computation. A lot of efforts in the past decades have been made for finding nearly uniform designs with $n \leq 50$ and $s \leq 20$. For example, Wang and Fang (1981) employed the good lattice point method, Fang, Shiu and Pan (1999) searched a nearly UD based on the most uniform Latin square, Winker and Fang (1998) employed the threshold accepting method to find nearly UDs. All the above authors chose the star discrepancy as measure of uniformity. The most up-to-date studies can refer to Fang, Ma and Winker (2001) and Fang and Ma (2001b). The uniform designs on the UD-web site are obtained by Fang *et al.* (2001) under the centered L_2-discrepancy.

4. Experiments with Mixtures

Many products are formed by mixtures of several ingredients, for example, building construction concrete consists of sand, water and one or more types of cement. Designs for deciding how to mix the ingredients are called *experimental designs with mixtures* that have played an important role in various fields such as chemical engineering, rubber industry, material and pharmaceutical engineering.

A design of n runs for mixtures of s ingredients is a set of n points in the domain

$$T^s = \{(x_1, \cdots, x_s) : x_j \geq 0,\ 1 \leq j \leq s,\ x_1 + \cdots + x_s = 1\}.$$

Due to the constrain $x_1 + \cdots + x_s = 1$, to find a design for experiments with mixtures is quite different from the factorial design where there is no constrain on the factors. A lot of designs have been proposed in the past such as the simplex-lattice design and the simplex-centroid design. Cornell (1990) and references therein gave a comprehensive review on designs of experiments with mixtures. Alternatively, Wang and Fang (1990) proposed the *uniform design of experiments with mixtures* (UDEM) that seeks experimental points to be uniformly scattered in the domain T^s. This section gives an introduction to the methodology of the uniform design of experiments with mixtures without/with constrains.

4.1. Uniform designs of experiments with mixtures

A uniform design of experiments with s-ingredient mixtures is a set of points that are uniformly scattered on the domain T^s. Wang and Fang (1990) employed the *transformation method* for construction of such uniform designs as following steps:

(a) Choose a uniform design, denoted by $\mathbf{U} = (u_{ki})$, $U_n(n^{s-1})$.

(b) Calculate $c_{ki} = (u_{ki} - 0.5)/n$, then

$$\{\mathbf{c}_k = (c_{k1}, \cdots, c_{k,s-1}), k = 1, \cdots, n\}$$

is a UD on $C^{s-1} = [0,1]^{s-1}$.

(c) Calculate

$$\begin{cases} x_{ki} = \left(1 - c_{ki}^{\frac{1}{s-i}}\right) \prod_{j=1}^{i-1} c_{kj}^{\frac{1}{s-j}}, \ j = 1, \ldots, s-1, \\ x_{ks} = \prod_{j=1}^{s-1} c_{kj}^{\frac{1}{s-j}}, \ k = 1, \cdots, n. \end{cases} \tag{4.1}$$

Then $\{\mathbf{x}_k = (x_{k1}, \cdots, x_{ks}), k = 1, \cdots, n\}$ is a uniform design on T^s.

Example 3. We give a UDEM for $n = 11, s = 3$. The first two columns of Table 3 forms a $U_{11}(11^2)$, the next two columns are c_1, c_2, a UD on $[0,1]^2$. Formula (4.1) for $s = 3$ has a simpler form as follows

$$\begin{cases} x_{k1} = 1 - \sqrt{c_{k1}}, \\ x_{k2} = \sqrt{c_{k1}}(1 - c_{k2}), \\ x_{k3} = \sqrt{c_{k1}} c_{k2}, k = 1, \ldots, n. \end{cases} \tag{4.2}$$

The results are listed in the last three columns of Table 3.

TABLE 3 *A UDEM for* $n = 11, s = 3$

$U_{11}(11^2)$		c_1	c_2	x_1	x_2	x_3
1	4	1/22	7/22	0.78680	0.14536	0.06784
2	9	3/22	17/22	0.63073	0.08393	0.28535
3	7	5/22	13/22	0.52327	0.19503	0.28170
4	1	7/22	1/22	0.43592	0.53844	0.02564
5	11	9/22	21/22	0.36040	0.02907	0.61053
6	3	11/22	5/22	0.29289	0.54640	0.16071
7	6	13/22	11/22	0.23129	0.38435	0.38435
8	8	15/22	15/22	0.17428	0.26273	0.56299
9	2	17/22	3/22	0.12095	0.75918	0.11987
10	10	19/22	19/22	0.07068	0.12673	0.80259
11	5	21/22	9/22	0.02299	0.57732	0.39969

4.2. Uniform design of experiments with restricted mixtures

However, in most experiments with mixtures some constrains have to be placed on the ingredients. For example, in making a cake, water and flour should be the major ingredients while sugar and milk have a small percentages. The constrains may be $0 \le a_i \le x_i \le b_1 \le 1, i = 1 \cdots, s$, or $\mathbf{0} \le \mathbf{a} \le \mathbf{x} \le \mathbf{b} \le \mathbf{1}$ where $\mathbf{a} = (a_1, \cdots, a_s)$, $\mathbf{b} = (b_1, \cdots, b_s)$ and $\mathbf{0}$ and $\mathbf{1}$ are vectors of 0's and 1's, respectively. In this case the experimental domain becomes

$$T^s(\mathbf{a}, \mathbf{b}) = \{\mathbf{x} : \mathbf{0} \le \mathbf{a} \le \mathbf{x} \le \mathbf{b} \le \mathbf{1}\}. \tag{4.3}$$

The domain $T_s(\mathbf{a}, \mathbf{b})$ is not empty if and only if

$$a \equiv \sum_{i=1}^{n} a_i < 1 < \sum_{i=1}^{n} b_i \equiv b.$$

The above condition may involve some superfluous constraints that can be removed by the following operation:

$$a_i := \max(a_i, b_i + 1 - b), \ b_i := \min(b_i, a_i + 1 - a). \tag{4.4}$$

Wang and Fang (1996) applied the transformation method for construction of uniform designs on $T^s(\mathbf{a}, \mathbf{b})$, but their method can not give a good design when some $d_i = b_i - a_i$ are very small. Recently, Fang and Yang (1999) employed the conditional method to propose an alternative method that can construct uniform designs for all cases. Let $\mathbf{x} = (X_1, \cdots, X_s)$ follow the uniform distribution over $T_s(\mathbf{a}, \mathbf{b})$. The Fang-Yang's method is based on the following facts:

(a) The distribution of X_i can be analytically expressed in a simple form;

(b) The conditional distribution of $X_1, \cdots X_{s-1}$ for given $X_s = x_s^*$ is the uniform distribution over $T^{s-1}(\mathbf{a}^*, \mathbf{b}^*)$ where $\mathbf{a}^*$ and $\mathbf{b}^*$ can be expressed in terms of $\mathbf{a}, \mathbf{b}$ and x_s^*.

For introducing our algorithm, let

$$\Delta_s = 1, \Delta_k = 1 - \sum_{i=k+1}^{s} y_i, k = s-1, \ldots, 2,$$

$$d_k = \max\{a_k/\Delta_k, 1 - \sum_{i=1}^{k-1} b_i/\Delta_k\}, k = s, s-1, \ldots, 2,$$

$$\Phi_k = \max\{b_k/\Delta_k, 1 - \sum_{i=1}^{k-1} a_i/\Delta_i\}, k = s, s-1, \ldots, 2,$$

$$G(u, d, b, c, k) = c\{1 - [u(1-b)^k + (1-u)(1-d)^k]^{1/k}\}.$$

Algorithm of generating a variate for the uniform distribution on $T^s(\mathbf{a}, \mathbf{b})$

Step 1: Generate $s-1$ random numbers $u_2, \cdots, u_s$;

Step 2: Let

$$x_k = G(u_k, d_k, \Phi_k, \Delta_k, k-1), k = s, s-1, \cdots, 2,$$

$$x_1 = 1 - \sum_{k=2}^{s} x_k,$$

Then $\mathbf{x} = (x_1, \cdots, x_s)$ is a sample for the uniform distribution on $T^s(\mathbf{a}, \mathbf{b})$.

Algorithm of generating a UD with restricted mixtures

Step 1: Choose a $U_n(n^{s-1})$, denoted it by $\mathbf{U} = (u_{ij})$;

Step 2: Calculate

$$t_{ij} = \frac{u_{ij} - 0.5}{n}, i = 1, \ldots, n, j = 1, \ldots, s-1;$$

Step 3: For each i, to apply the above algorithm with $(t_{i1}, \ldots, t_{i,s-1})$ as $u_2, \ldots, u_s$ and to calculate

$$x_{ik} = G(t_{ik}, d_k, \Phi_k, \Delta_k, k-1), k = s, s-2, \ldots, 2,$$

$$x_{i1} = 1 - \sum_{k=2}^{s} x_k,$$

Then $\{\mathbf{x}_i = (x_{i1}, \ldots, x_{is}), i = 1, \ldots, n\}$ is a UD with restricted mixtures over $T^s(\mathbf{a}, \mathbf{b})$.

Example 4. Consider an experiment with mixtures in a pharmaceutical study where it is necessary to dissolve a slightly polar drug in a mixture of water and two cosolvents, ethanol and propylene glycol, to increase the drug's solubility. It is also of interest to know whether and where a maximum exists in the solubility profile of the drug in the mixture of solvents.

The three factors, ethanol (x_1), propylene glycol (x_2) and water (x_3) are chosen with the domain $T_3(\mathbf{a}, \mathbf{b}) = \{\mathbf{x} = (x_1, x_2, x_3) : 0.0463 \leq x_1 \leq 0.7188, 0.0272 \leq x_2 \leq 0.5776, 0.2272 \leq x_3 \leq 09265, x_1 + x_2 + x_3 = 1\}$. The response measured is the vapor pressure (y) (mm Hg).

Suppose that we want to put 12 experimental points uniformly scattered on this domain. Applying the above algorithms to the case where $n = 12$ and $s = 3$, we can obtain a UD with restricted mixtures over $T_3(\mathbf{a}, \mathbf{b})$. The 12 points and the corresponding responses obtained are shown in Table 4.

TABLE 4 *Design and responses in Example 4*

No.	x_1	x_2	x_3	y
1	0.12296	0.11323	0.76381	31.5042
2	0.35453	0.04379	0.60168	51.5640
3	0.24176	0.36565	0.39259	30.0888
4	0.26535	0.47616	0.25849	28.9297
5	0.05914	0.41827	0.52258	21.5290
6	0.55981	0.07786	0.36233	56.6437
7	0.52303	0.22904	0.24793	44.9973
8	0.20319	0.18860	0.60821	36.6152
9	0.11576	0.54129	0.34296	20.3480
10	0.40656	0.15008	0.44336	45.6282
11	0.14105	0.27173	0.58723	30.8623
12	0.33631	0.31707	0.34662	37.0407

We consider the second-order centered quadratic regression model. By using model selection techniques, the final model is

$$\begin{aligned}\hat{y} = {} & 37.3126 + 84.6285(x_1 - 0.2775) \\ & +84.0939(x_1 - 0.2775)(x_3 - 0.4565) \\ & +40.9079(x_3 - 0.4565) \end{aligned} \tag{4.5}$$

with $R^2 = 98.94\%$ and $s^2 = 1.8969$. Then we maximize y with respect to $x_i, i = 1, 2, 3$ under models (4.5) over the domain $T_3(\mathbf{a}, \mathbf{b})$, and find that $\max \hat{y} = 59.2179$

at the point $x_1 = 0.7188, x_2 = 0.0272, x_3 = 0.2540$. By some additional experiments at the ingredient-combination $x_1 = 0.7188, x_2 = 0.0272, x_3 = 0.2540$, the average of vapor pressure is 61.75.

5. Statistical Models and Applications of Uniform Designs

5.1. Statistical models

There are different models to explain the usefulness of uniform design. The overall mean model that wants to estimate the overall mean of the response over the region has been widely used in computer experiments. Under model (1.7) the overall mean of y on $\mathcal{T}$ is

$$\mu = \int_{\mathcal{T}} g(x_1, \cdots, x_s) dx_1, \cdots, dx_s.$$

By a linear transformation, we can assume $\mathcal{T}$ is the unit cube $C^s = [0,1]^s$ in R^s. The sample mean,

$$\bar{g}(\mathbf{x}) = \frac{1}{n} \sum_{i=1}^{n} g(\mathbf{x}_i),$$

of a set of points determined by the design, $\mathcal{P} = \{\mathbf{x}_1, \cdots, \mathbf{x}_n\}$ on C^s, is an estimator of μ. The Latin hypercube sampling proposed by Makey, Beckaman and Conover (1979) can provide an unbiased estimate of μ with variance $O_p(n^{-1/2})$ as $n \to \infty$. From the Koksma-Hlawka inequality (p. 18, Niederreiter, 1992)

$$|\bar{\mathbf{x}} - \mu| \leq V(g) D(\mathcal{P}) \tag{5.1}$$

where $V(g)$ is the variation of g on C^s in the sense of Hardy and Krause (p. 19, Niederreiter, 1992) and $D(\mathcal{P})$ is the star discrepancy of $\mathcal{P}$ (p. 14, Niederreiter, 1992), it indicates that a set $\mathcal{P}$ with smallest discrepancy for given n provides a good design for estimating the mean μ, *i.e.*, $\mathcal{P}$ is a UD. The overall mean model is the most popular one for justifying the Latin hypercube sampling as well as for uniform design, see Fang and Wang (1994) and Hickernell (1998, 1999) for the details. Wiens (1991) considered an approximately linear model and obtained two optimality properties of uniform designs. Xie and Fang (2000) showed that the uniform design is minimax and admissible in a certain model while Hickernell (1999) pointed out the uniform design is a robust design. Recently, Lam, Welch and Young (2002) in study on screening for drug discovery proposed so-called uniform coverage designs and suggested some criteria for evaluating designs.

5.2. Applications

Hundreds of case studies (see the UD web site) show wide applications of the uniform design in various fields. Most of them are in industrial experiments. There are also many applications of uniform designs to computer experiments. Fang *et al.* (2000), Fang and Lin (2002) and Li (2002) gave a detailed discussion and showed some case studies. Atkinson *et al.* (1998) discussed the possibility of the use of D- and T-optimum designs to the kinetics of reversible chemical reaction. Xu, Liang and Fang (2000) gave comparisons among D-optimal, orthogonal, and uniform designs for this chemical reaction and found that the uniform design is the robust. Liang, Fang and Xu (2001) gave a comprehensive review on applications of UD in chemistry and chemical engineering.

In the literature, the uniform design can be utilized as
- an industrial design with model unknown,
- a space filling design for computer experiments,
- a robust design against the model specification, and
- a design of experiments with restricted mixtures.

Advantages of uniform designs include
- more choices for the users,
- designs have been tabulated,
- both industrial and computer experiments can be applied, and
- less information of the underlying model is required.

6. Relationships Between Uniform Designs and Orthogonal Designs

The orthogonal design (OD for short)is a kind of fractional factorial designs and has been widely used for various fields. An OD is an orthogonal array of strength two and is defined by

Definition 6.1. *An orthogonal design table $L_n(q^s)$ (OD table for short) is a U-type design $U(n;q^s)$ such that all level-combinations in any two columns of the table appear equally often.*

It is clear that the OD requires one- and two-dimensional projection uniformity of experimental points over the domain (in the sense of balance among

level combinations) while the UD asks for one-dimensional and overall uniformity. Fang *et al.* (2000) found that many OD tables are UD ones under the centered L_2-discrepancy. Later, Ma, Fang and Lin (2002) give some theoretic results on relationships between uniformity and orthogonality.

There are many useful criteria for comparing factorial designs, such as resolution (Box, Hunter and Hunter, 1978) and minimum aberration (Fries and Hunter, 1980). For given a regular factorial design D of s factors, its word-length pattern, denoted by $W(D) = (A_1(D), \cdots, A_s(D))$, gives rich information on its statistical inference ability. The resolution and minimum aberration are defined based on the word-length pattern. The reader can refer Dey and Mukerjee (1999) for details of these criteria and concepts. For a two-level regular design D its word-length pattern can be determined by the Hamming distances among the rows of the design matrix $\mathcal{P}_D$. It is interesting to note that the CD of the experimental points of D can be expressed as a function of the Hamming distances of the points. This fact was discovered by Fang and Mukerjee (2000) who obtained an analytic link between the uniformity and word-length pattern for any regular two-level factorials 2^{s-p}. They showed

$$[CD_2(D)]^2 = \left(\frac{13}{12}\right)^s - 2\left(\frac{35}{32}\right)^s + \left(\frac{8}{9}\right)^s \left\{1 + \sum_{i=1}^{s} \frac{A_i(D)}{9^i}\right\}.$$

The above formula indicates that 1) the uniformity criterion is essentially consistent with the resolution and minimum aberration criteria; 2) the uniformity can be applied to any factorial design, but the resolution and minimum aberration can be applied only to regular designs. The above link can be extended to factorials with more levels.

Two orthogonal designs are called isomorphic if one can be obtained from the other by relabeling the factors, reordering the runs and switching the levels of the factors. For identifying two $L_n(q^s)$ designs, a complete search compares $n!(q!)^s s!$ designs from the definition of isomorphism. Therefore, to identify the isomorphism of two $d(n, q, s)$ designs is known to be an NP hard problem when n and s increase. Obviously, two isomorphic designs have the same uniformity and projection uniformity distribution. By the use this fact Ma, Fang and Lin (2001) proposed a powerful algorithm for detecting non-isomorphic orthogonal designs.

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