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ARTICLE

Strategies using of Design of Experiments (DOE) techniques: In view of a Review

Basma Yahya Alashwal¹, Mohamed Saad Bala¹, Arun Gupta^{1*}, Triveni Soubam¹

¹ Faculty of Chemical & Process Engineering Technology, Universiti Malaysia Pahang, Lebuhraya Tun Razak, 26300 Gambang, Kuantan, Pahang, Malaysia.

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ABSTRACT

There Design of Experiment (DOE) has developed into a valuable collection technique for statistical and mathematical processes used in modelling and analysis of problems involving multiple variables influencing the desired response. Numerous researchers and engineers use this technique in a variety of fields, including botany, pharmaceuticals, biotechnology, and other engineering disciplines. This review article summarised key points from the Design of Experiments Using Response Surface Methodology (RSM). Design of experiments (DOE) has guidelines and procedures, but the literature does not recommend a specific method for finding and selecting the best possible design from a large number of possible designs.

1. Introduction

Optimization is the study of the effects of various variables on an experiment in order to determine the best conditions for obtaining the best possible results. As a result, complex operations with a large number of variables influencing the desired response necessitate a proper experimental design (Behera et al., 2018). The design of experiments (DOE) is a scientific research technique used to plan and analyse experiments. This method can obtain sufficient data with a small number of investigations because it allows for the simultaneous and continuous change of several experimental parameters over an extended period.

A mathematical model of the procedure under investigation is developed based on the information gathered (Whitford et al., 2018). The model can determine the effect of experimental parameters on the outcome and the optimum state of the process. Custom software enables the development of experimental designs, the generation of models, and generated data visualisation. A DOE approach can significantly boost screening efficiency for suitable experimental conditions (Raza et al., 2018; Fu et al., 2017).

On the other hand, experiments are used to evaluate the performance of processes and systems. Figure 1 illustrates a diagram of a procedure or system. A process is a collection of machines, methods, people, and other resources that convert the input to output with one or more observable responses and in which variables can be controlled (x_1, x_2, \dots, x_q) or uncontrollable ($z_1,$

* Corresponding author.

E-mail address: arun@ump.edu.my (Arun Gupta)

z_2, \dots, z_q). The objective of conducting experiments may include the following (Roci, 2016):

- To determine which variables, have the most significant influence on the response y .
- To choose where to place the influential x 's to bring y close to the desired nominal value.
- To decide where to place the influential x 's to keep the variability in y to a minimum.
- It is necessary to determine where to place the influential x 's to minimise the effects of the uncontrollable variables.

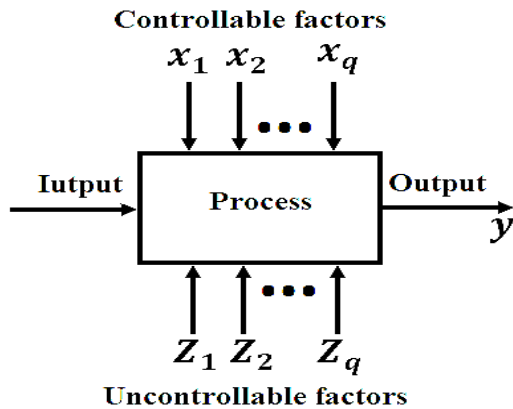


Figure 1 General model of a system in RSM.

2. The design of experiments (DOE) selection

2.1. One Factor at A Time (OFAT) method

There are various strategies to optimize the financial product, such as one-factor-at-a-time (OFAT) and a statistical approach called the design of experiment (DOE). OFAT is a technique for determining how a change in one factor can affect the output when all other factors remain constant. This method is incapable of examining variable interactions and is highly time-consuming. On the contrary, the statistical approach (DOE) is the best method because it enables researchers to evaluate the interactions between multiple variables and shortens the duration of the study (Whitford et al., 2018).

2.2. Full Factorial Design (FFD)

Factorial designs are frequently used in experiments in which multiple variables must be investigated to determine a specific response. Due to researchers' widespread use and role as a foundation for additional valuable planning, exceptional factorial design cases are critical (Piepho et al., 2018). The number of levels for each parameter is limited to two in these factorial designs. The number of experiments is reduced by limiting the levels to two and doing a complete factorial experiment, which allows all the variables and their interactions to be investigated.

If all of the variables are quantifiable, the data from such trials may be utilised to predict outcomes if a linear model is employed to represent the response (Adepoju et al., 2016).

The interaction model development and screening of the experiments were facilitated using these factorial designs. FFD method is used for many reasons (Roci, 2016):

- It requires a small number of runs for each factor under investigation.
- It can be upgraded to create composite designs for optimisation purposes.
- It serves as the foundation for the experiment design using the Two-Level Factorial, which is extremely useful during the early stages.

In general, a Two-Level Factorial Design has a high and a low level of significance for each factor. An orthogonal array of experiments is constructed for analysis when using the selected parameters. Factors are typically represented by the numbers +1 or -1. The number of times it will be replicated will be indicated by 0 (Rezende et al., 2018).

There are two factors in the 2^k factorial design, A and B, each with two levels. These levels are frequently classified into low and high values. When discussing 2^2 planning, it is customary to label A and B factors as "low" and "high" using (-) and (+) signs, respectively. The 2^2 -step planning process is depicted in Figure 2. When representing "plans" geometrically, $2^2 = 4$ runs, or experiment combinations, form the square's vertices. This is sometimes referred to as the "geometric concept for planning." (Sanchez et al., 2009). Geometrically, the experimental design may be interpreted as a square, as shown in Figure 2 (A). As shown in Figure 2.11 (B), each row in the experimental design corresponds to one experiment (Roci, 2016).

The factorial design with two levels indicated 23 at three factors. It was constructed similarly to the factorial design with two levels in two factors. Figure 3 (A) illustrates the eight experiment combinations as a cube geometrically. Figure 3 (B) shows the design matrix for the eight experiment combinations.

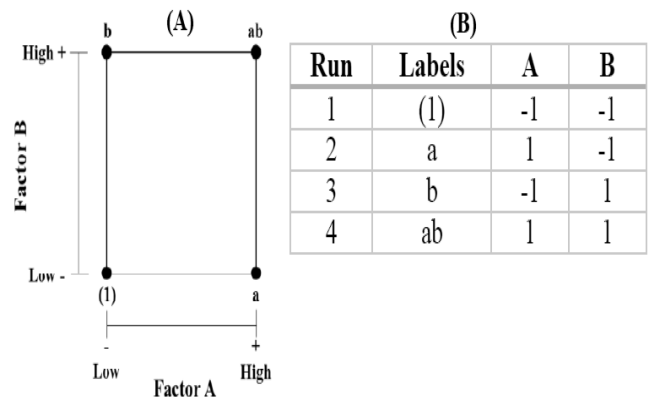


Figure Error! No text of specified style in document. The experimental design interpreted as a square.

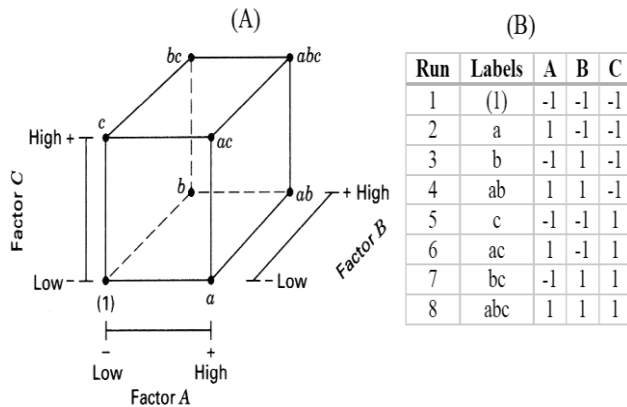


Figure 3 The matrix design of eight combinations of treatment.

2.4. Response surface method (RSM)

Nowadays, the response surface method has got a paramouncy in the statistic subject of the design of the experiments, which has useful collection techniques of statistical and mathematical processes for modelling and analysing the problems in which several variables influence the response to be optimised. Many researchers and engineers are employing this method in various fields, including botany, pharmaceuticals, biotechnology, and other engineering disciplines (Bowden et al., 2019). Typically, the optimisation process includes the following procedures (Aydar, 2018):

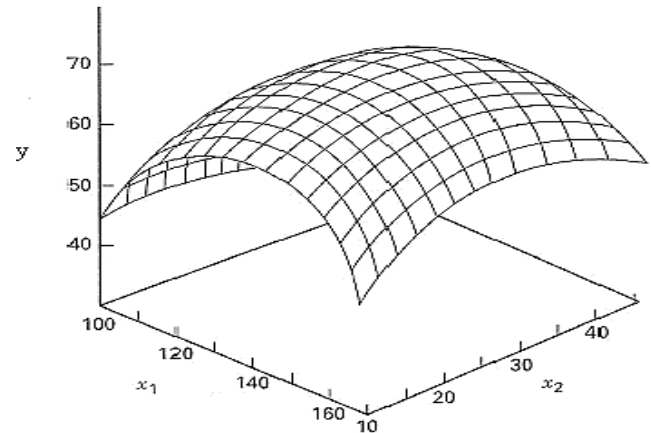
- The independent variables are determined based on prior knowledge or experience or from the literature.
- The screening process is used to select a suitable model based on the factor results.
- Experiments are designed and carried out.
- ANOVA examines the responses, analyses on lack of fit to obtain an empirical mathematical model for all responses.
- The responses were screened using a variety of criteria to determine the values of independent variables.

2.5 Central composite design (CCD)

The CCD tool in RSM is used in the optimisation process. CCD consists primarily of three essential steps: conducting statistically designed experiments, estimating the coefficients in a mathematical model, predicting the response, and determining the model adequacy (Sadhukhan et al., 2016).

Generally, a graphic representation of the response surface is possible. The contours of a response surface, such as ridgelines, hills, and valleys, are represented by the graph. Thus, the function $f(x_1, x_2)$ can be plotted against the values of x_1 and x_2 to demonstrate their relationship as illustrated in Figure 4 (Bradley, 2007).

Figure 4 Shape of a response surface graph.



The standard error remains constant throughout this design CCD, remaining equidistant from the region's centre. The following explains the rotatability criterion: Let $(0, 0, \dots, 0)$ represent the centre of the area where the relationship between Y and X is being studied. The standard Y error can be determined using the experimental data at every location on the fitted surface. This standard error is proportional to the x I coordinate of the area. Due to the rotatability criterion, this common error is constant for all central issues to the region's centre and all positions meeting the following equation (1) (Gautam et al., 2020):

$$x_1^2 + x_2^2 + \dots + x_k^2 = \rho^2 = \text{constant} \quad (1)$$

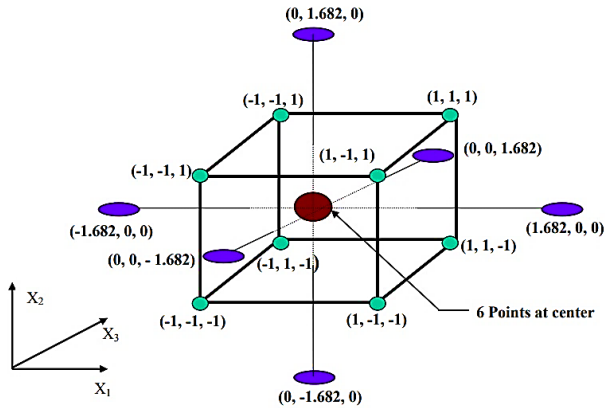
The central composite design (CCD) is a rotatable design divided into three sections, which have points as follows (Gopal et al., 2018):

- Points 2^k Design, where k is the number of the factors, and 2 is the number of the settings marked during the experiments.
- Star points (extra points) were placed on the coordinates axes to form the central composite design with a star arm of size α .
- Fewer points were put on the centre to give roughly equal precision for response Y with a radius circle equal to one.

The factor α is the process or sphere radius of the star points positioned on it. While the size of the experiment is dropped by half replica of 2^k factorial design at $k \geq 5$. At half replica, α turns into $2^{k-1/4}$. Furthermore, the replication is not required to determine the square of an error average because it is possible to be determined by duplicating the centre points. However, the second-order components of central composite rotatable design (CCD) for the diverse variables were presented in Table 1 to facilitate the process of the design. A graphical illustration for the other areas of the case of three variables has shown in Figure 5 (Gautam et al., 2020).

Table 1 The central composite design (CCD) components second-order.

Variables k	Factorial Points 2^k	Star Points 2^k	Centre Points n	Total N	Value of α
3	8	6	6	20	1.682
4	16	8	7	31	2.000
5	16	10	6	32	2.000
6	32	12	9	53	2.378

**Figure 5** Central composite rotatable design in 3X-variables.

2.6 Experimental designs for fitting response surface

The most effective way to estimate model parameters is to collect data using appropriate experimental methods for fitting response surfaces. The following are some of the characteristics of an ideal response surface design (Roci, 2016):

- ❖ Allows designs of a higher order to be built up one by one.
- ❖ Gives a good picture of the variance in predictions across the area where the experiment is taking place.
- ❖ Allows for some protection against outliers or missing values, but not much.
- ❖ Does not need a lot of runs.
- ❖ Does not need too many levels of the independent variables to get the job done
- ❖ Makes it easier to figure out the model's parameters.
- ❖ A reasonable number of data points are spread out across the area of interest.
- ❖ Allows model adequacy and a model that does not fit to be investigated.
- ❖ Gives an estimate of how much error.
- ❖ It gives very accurate estimates of the model coefficients.

3. Conclusion

In summarized of this paper, after going through the related literature review, it was observed that using strategies using of Design of Experiments (DOE) techniques suggested applying with several potential applications. DoE is becoming more accepted as a valuable tool for process improvement in the pharmaceutical industry. When experiments and analyses are repeatable, the time it takes to generate useful data can be reduced by half or more. They are used to predict the preferred settings, and these settings can then be implemented, in order to verify the model. They must work together to ensure that the DoE parameters selected are feasible, repeatable, and relevant to the overall project objectives. A growing number of businesses are relying on DoE to help them develop more efficient processes.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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