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Review Article

Casting a Spotlight on Factorial Design: Exploring the Power of DoE for Experiment Screening and Optimization: A Review

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ABSTRACT

Design of Experiments (DOE) is a powerful and systematic approach used in various fields to efficiently plan, execute and analyze experiments. This review provides a comprehensive overview of the application of DOE in the context of screening and optimization of experiments. Screening experiments are employed to identify significant factors or variables that influence a response, while optimization experiments aim to fine-tune these factors to achieve optimal outcomes. The review introduces the fundamental concepts of DOE, including factors, levels and response variables. It explores the various types of designs commonly used in screening, such as full factorial, Taguchi and Plackett-Burman designs, highlighting their advantages and limitations. The article also delves into the practical aspects of designing and conducting experiments with DOE, emphasizing the importance of proper planning and statistical analysis. Key topics covered include the selection of appropriate designs, sample size determination and data analysis techniques. Furthermore, the review touches upon the integration of computer-aided tools and software for DOE, making the process more efficient and accessible. The review also discusses the impact of DOE on resource and time savings, as well as its potential for enhancing product quality and process efficiency. This review underlines the significance of Design of Experiments in screening and optimization, offering insights into its versatility, practical implementation and the substantial benefits it can bring to research and industry. Researchers, practitioners and decision-makers in various domains will find this review valuable in harnessing the full potential of DOE for improving experimentation and decision-making processes.

Keywords: DoE (Design of Experiments), Experiment Screening, Factorial Design, Optimization, Plackett Burman design, Taguchi method.

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INTRODUCTION

"DoE" constitutes a structured methodology for establishing the connection between independent variables related to products or processes and how they influence the response variable associated with those products or processes.[1]

Experiment design are incredibly necessary, if we want to undertake well planned out study of very difficult system, if study is not arranging adequately.[2] Then collected data will be completely incorrect and cannot anticipate a statistical basis for analysis and conclusion. Many software applications have the ability to generate numerous types of designs, yet most of us are unaware of how software generates these diverse types of designs. It is incredibly informative and fascinating to grasp the idea behind how the designs are created. To attain success, employ statistical techniques to methodically explore the connection between a system's inputs and outputs. To identify critical design variables (screening)-various inputs such as carbon, pH, temperature, agitation time, surfactant, polymers, etc. Product yield, particle size and entrapment efficiency could all be outputs. They all react differently to outputs. Inputs are referred to as x independent variables and outputs are referred to as y dependent variables.

To determining whether a factor or set of factors has an effect on the response. Used examine whether variables interact in their effects on the response. To simulate the response's behavior as a function of the variables.[3]

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The optimization using DoE helps in reducing cost, saving time, preventing errors and helps in reproducibility.

Common Terms in DoE

Factors/Cause (Independent variable)

Also called control factors which we can control and May (interaction) or do not necessarily have an impact on each other. Explanatory variables that can be changed (excipients and concentrations).

Response/Effect (Dependent variable)

Measured output value (Results). Depends on independent variables.

Levels

Specific values of factors (inputs) (2 or more) these high and low levels can be generically coded as +1, -1 and 0 as center level

History of Experimental Design and Analysis

Factorial and fractional factorial designs (1920+)-Agriculture.

Sequential designs (1940+)-Defense.

Response surface designs for process optimization (1950+)-Chemical.

Robust parameter design for variation reduction (1970+)-Manufacturing and Quality Improvement.

Virtual (computer) experiments using computational models (1990+).[4]

Optimize product or process design

The term optimize is defined as "To make perfect". It is the process of determining the optimum method to use available resources while considering all of the factors that impact decisions in every experiment. The process of minimizing raw materials and obtaining the maximum amount of desired product is known as optimization and the product's quality will be improved. To achieve robust performance always Y should not go out of control when X changes slightly.[5] For example, if temperature changes by one degree, output should not a large change; this is referred to as robust design. Without DoE, it is impossible to jump from small scale to large scale, to expect optimum process and to develop regression relationships.

Cause and Effect

To create Correspondences like, Y-Yield of our preferred product (output) is equal to function of various input parameters like X1, X2 and X3. Experiments that demonstrate cause and effect are required. Y=fn (x1, x2, x3 ...) is more efficient than a standard approach of changing "one variable at a time". OFAT (one factor at a time) is unable to detect interactions. Unless there are simultaneous changes.[6] It is not possible to study the interactions as well as the various mathematical relationships between various input parameters and output parameters.

Comparison/control

Experiments that are good are always comparative. For example, i) compare blood pressure in volunteers treated with placebo (or an existing drug) to blood pressure in volunteers treated with a new drug. ii) A comparison of blood pressure in male and female volunteers who were both given the drug. In this case experimental group is pitted against concurrent controls (rather than to historical controls). To introduce a new drug to the market, always should conduct a clinical trial with the old drug for one set of volunteers and the new drug for another set of volunteers.

Replication

Repeating the entire experiment twice or three times, not just once, because this provides information about the error and calculating the error sum of squares without replication is difficult.[7] Assume comparing blood pressure levels in the control and treatment groups. It is simply a bad idea to conduct the experiment with only one volunteer, one of each. Since the experiment lacks awareness of the error. As a result, it is critical. Limit the impact of uncontrolled variation (i.e. increase precision), Uncertainty should be quantified. Replication is the same as reproduce, but it is not the same as repeat. As a result, replication can assist in determining the error margin.

Randomization

Subjects participating in experiments should be allocated to treatment groups through a random process. Randomization, in this context, doesn't imply a careless or arbitrary approach. Instead, it entails a deliberate and systematic method, such as using a computer, coins, dice, or cards, to ensure the randomness of the allocation. We have to randomize otherwise we will always have a bias. Randomization enables us to leverage probability theory, providing a robust basis for conducting statistical analyses.[8] Techniques used like simple random sampling, stratified random sampling, systemic sampling, multi-stage sampling, multi-phase sampling and cluster sampling.

Stratification/Blocking

Blocking is a mathematical strategy for removing variance induced by an identified change throughout the course of an experiment. For example, you may need to employ two distinct raw material batches to finish the experiment, or the experiment may need multiple shifts or days to complete. The modification may cause the response data to move in each of these scenarios. Blocking eliminates this shift, thus "normalizing" the data.

Example: Attempting to assess the impacts of coating process variables such as speed, temperature and pressure on the tensile and elongation qualities of your product. You will need to utilize two distinct batches of raw material due to the amount of runs required. You anticipate that differences in the raw material will affect the reaction, but you are not interested in investigating that impact at this moment. As a result, raw material is NOT a consideration and you should instead block on it. This will eliminate the raw material influence on tensile and elongation from the ANOVA, allowing you to focus on the other factor effects.

Interaction

An interaction is when the effect of one factor on a response variable depends on the level or settings of another factor. The main effect describes how a factor influences a product response.[9] However, this influence can be contingent on the values or states of other factors, which is commonly referred to as an "interaction". In most circumstances, two-factor interactions, such as AB, AC and BC, will be significant. In rare cases, three-factor interactions such as ABC, ACD, BCD and ABD are substantial. This type of interaction is also known as a high-order interaction for example, the effect of temperature and pH on product yield may vary when pH is at its low level from when pH is at its high level. There are three possible types of interactions.

The two lines depict the outcomes of product yield, with one line representing Factor B at its high level (blue) and the other at its low level (red). Notably, these two lines are almost parallel, indicating the absence of any interaction among the factors. So, the effect of temperature and pH on product yield is additive fashion.

The Figure 1 illustrates the second type of interaction. In this case, the lines are no longer running in parallel. Instead, there is a discernible moderate interaction between the factors. Specifically, the impact of temperature on product yield is more pronounced when Factor B is at its low level compared to when Factor B is at its high level. In other words, the slope of the increase in product yield is steeper when Factor B is at its low level than when it's at its high level.

The Figure 1 demonstrates the presence of a strong interaction, which is the third type observed. In this scenario, when Factor B is at its low level, there is a decrease in product yield as Factor A increases. Conversely, when Factor B is at its high level, an increase in Factor A leads to an increase in product yield.

Main effects

An effect is quantified as the mean response when a factor is at its maximum level subtracted from the mean response when it is at its minimum level, while keeping all other factors persistent

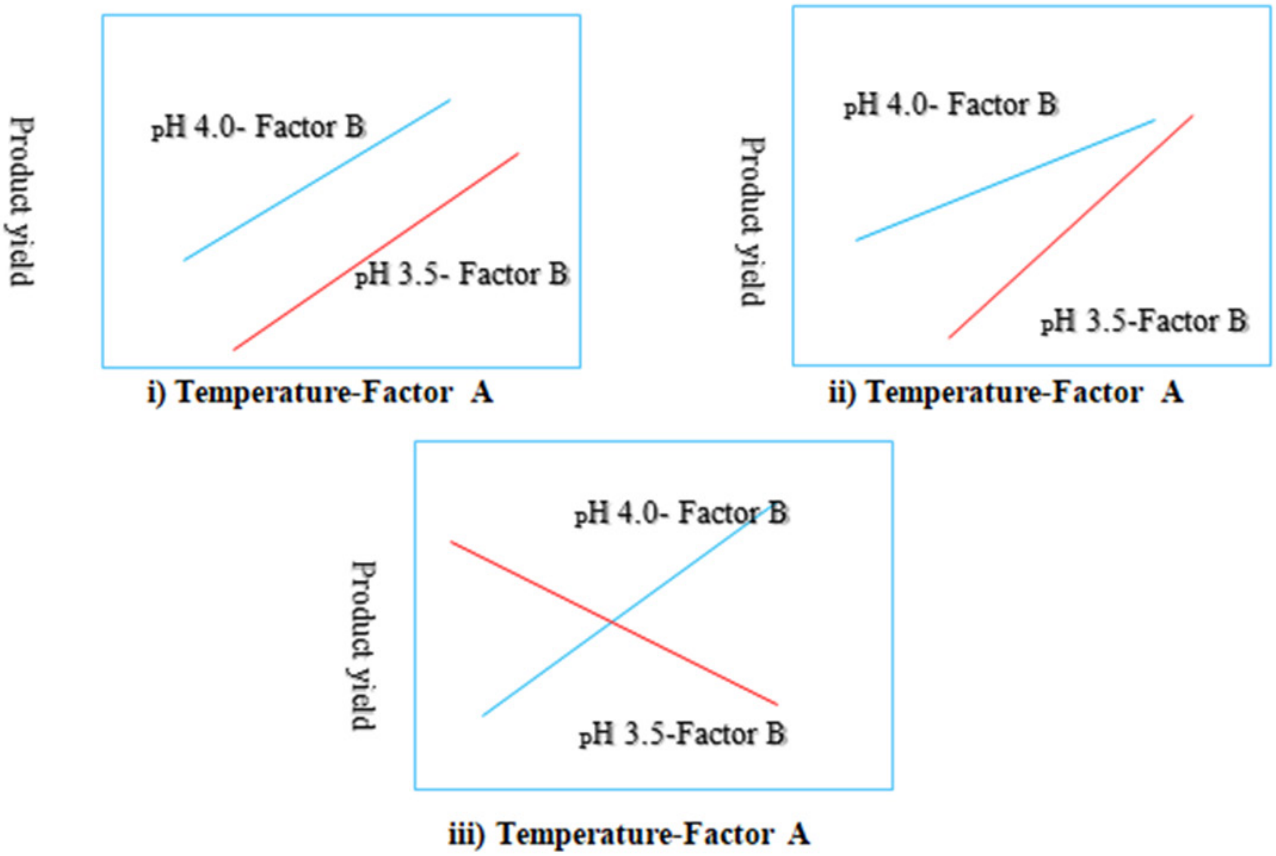


Figure 1: Interaction effect between factors.

in Table 1. It is the particular effect of a factor or independent variable in the absence of other parameters in the experiment.[10] The influence of one independent variable averaged over all levels of another independent variable. It tells if the average response value is increasing or decreasing. A significant main effect denotes a significant difference between at least two main effect means for the factor.

Algebraically, the main effect of temperature is given by:

$$(Y3 + Y4) - \frac{Y1 + Y2}{2} = (47.7 + 79.5) - \frac{58.3 + 46.2}{2} = 11.35$$

This implies that the mean product yield rises by 11.35 when the reactor temperature transitions from its lower level to its higher level.

The main effect of time is given by:

$$(Y2 + Y4) - \frac{Y1 + Y3}{2} = (46.2 + 79.5) - (58.3 + 47.7)/2 = 98.5$$

This signifies that, as the reactor time escalates from its base level to its upper level, the average product yield experiences a growth of 9.85.

Mathematically, the interaction between temperature and residence time can be represented as the average difference between the effect of residence time at the high temperature level and its effect at the low temperature level:

$$(79.5 - 47.7) - \frac{46.2 - 58.3}{2} = 21.9$$

Mathematically, the interaction between temperature and residence time can be expressed as the average difference between the effect of temperature at the high level of residence time and the effect at the low level of residence time:

$$(79.5 - 46.2) - \frac{47.7 - 58.3}{2} = 21.9$$

Experimental design techniques are used to determine the main effects and interactions. We have determined the following so far:

Main Effect of Temperature=11.35

Main Effect of Residence Time=9.85

Interaction between Temperature and Residence Time=21.9

Types of Design of Experiment

2-Level-Factorial Design

Factorial designs are a type of experimental design that, in general, provides a great quantity of valuable knowledge from a limited number of trials. When the number of experiments available is restricted, factorial designs provide an efficient method of obtaining the most knowledge from these studies.

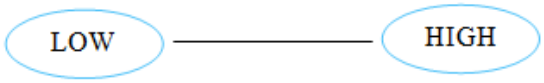
This design is mostly used to screen the significant influences on the product. Factorial designs enable the instantaneous investigation of the influence that various elements may have on a process.[9] When conducting atrial, adjusting the amounts of the components concurrently rather than one at a time saves time and money while also consenting for the investigation of interfaces between the variables. The formula=(levels)^{Factors} may be used to compute the number of runs. The letter k is used to represent factors. It is the most effective experimental design for two-level factors. It will produce averaged results without the requirement for replication. It will take into consideration interactions. It provides a more sensible optimization approach in a steepest ascent. The classification of Design of Experiments illustrated in Figure 2.

2-level one-factor design

Two-level factorial designs in Table 2 are applicable for estimating models that encompass first-order effects. (e.g. b_1x_1) and interaction effects (e.g. $b_{12}x_1x_2$). Models with second- or higher-order variables in a single factor cannot be fitted using two-level factorial methods. This constraint arises due to the necessity of conducting experiments with three or more levels of a single factor to detect curvature in that factor, a requirement which two-level factorial designs (by their very definition) fail to meet. Therefore, two-level with one factor cannot be used to estimate high-order interactions. This level was used to investigate only the main impact rather than interaction.[11]

A

21=2 runs



2 levels

Table 1: Experimental design data.

	Factors (X)		Response (Y)
Runs	Time	Temp	Product Yield
1	80	170	58.3
2	90	170	46.2
3	80	180	47.7
4	90	180	79.5

2-level Multi factor design

Higher-order interaction effects can be estimated using two-level multifactor factorial methods (e.g. $b_{123}x_1x_2x_3$). One significant part where such interactions are commonly originate is in kinetics and pharmaceutical formulations, where three-component rate expressions occur, for example, Rate=k[A][B][C]=$b_{123}x_1x_2x_3$. Nevertheless, in most domains, interactions beyond the second order (third or high-order) are infrequently observed.

2-level two-factor design (2^2)

These designs find application in both formulation development and the assessment of method ruggedness or robustness across a specific range. They consist of two variables, each having two levels. The total number of potential combinations is determined by multiplying the levels of each variable. Each specific pairing of factors and their respective levels is referred to as a treatment combination. So, if two variables are present at two levels, there are 2×2=4 treatment combinations.[12]

The four experiments in the Table 3 may be expressed as (1)=both factors are at the base level, a=factor at the high level, b=factor at the high level and ab=both factors at the high level. Multiply both variables as stated above to derive interaction from the experiment. Furthermore, the number of high and low levels in each column is highly symmetric.

2-level 3-Factor design (2^3)

The eight experiment in Table 4 expressed as (1)=three factors are at the base level, a=factor at the high level, b=factor at the high level, (c)=factor at the high level, ab=both factors at the high level, ac=both factors at the high level and bc=both factors at the high level and abc=three factors at the high level. All these designs are balanced and orthogonal. This design is also called balanced design. The balance and orthogonally is very important to perform strategy of design

Full factorial design

Number of Runs for a 2^k full factorial design. In full factorial design number of experiments will be huge (Table 5).[13]

If we take two factors, such as a and b, we do four experiments or runs in full factorial design. Examining the main effects of a and

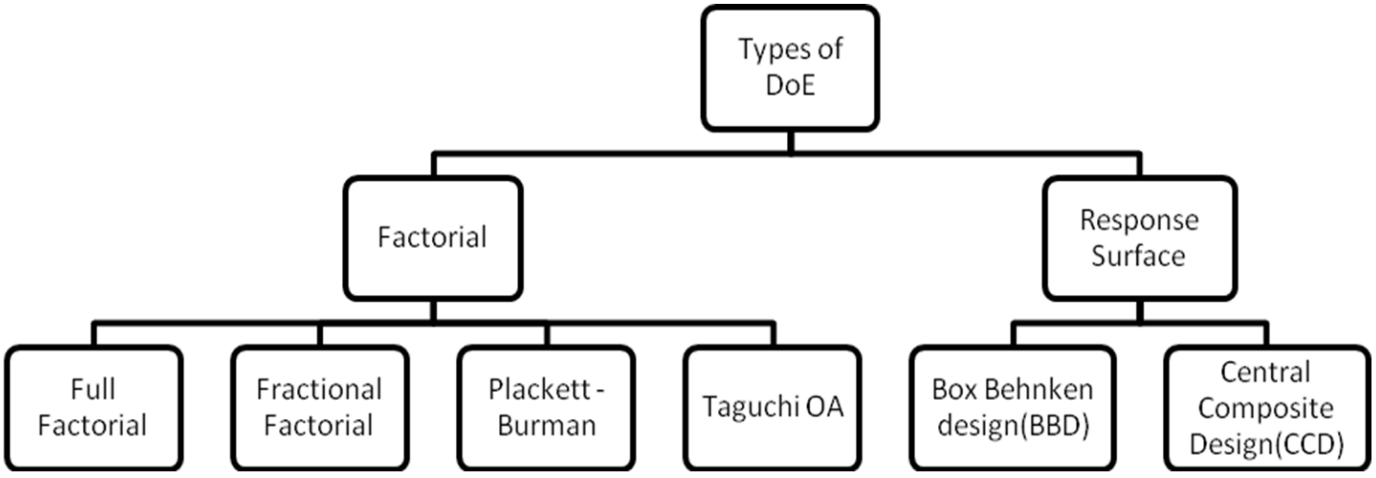


Figure 2: Classification on types of Design of Experiment.

Table 2: 2-level one-factor design.

Runs	Tc	Factors-A
1	1	+1
2	a	-1

Tc-Treatment combinations; +denotes=high level; -denotes=low level.

Table 3: Two-level two-factor design.

Runs	tc	Factors		Interaction
		A	B	AB
1	(1)	-1	-1	+1
2	a	+1	-1	-1
3	b	-1	+1	-1
4	ab	+1	+1	+1

Table 4: Two-level Three-Factor design.

Runs	tc	Factors			Interaction			
		A	B	C	AB	AC	BC	ABC
1	(1)	-1	-1	-1	+1	+1	+1	-1
2	a	+1	-1	-1	-1	-1	+1	+1
3	b	-1	+1	-1	-1	+1	-1	+1
4	ab	+1	+1	-1	+1	-1	-1	-1
5	c	-1	-1	+1	+1	-1	-1	+1
6	ac	+1	-1	+1	-1	+1	-1	-1
7	bc	-1	+1	+1	-1	-1	+1	-1
8	abc	+1	+1	+1	+1	+1	+1	+1

Table 5: Full factorial design.

Number of factors	Number of runs
1	2
2	4
3	8
4	16
5	32
6	64
7	128
8	256
9	512
10	1,024
15	32,768
20	1,048,576

b as well as one interaction between ab, also known as a second order interaction. Assume we have three variables, a, b and c. there are three main effects like a, b and c, then three second order interaction like ab, ac and bc and we can also have third order interactions between (abc) in Table 6.

In the event that we have four variables or factors (a, b, c and d). The experiment has four main effects (a, b, c and d), as well as six two-way interactions (ab, ac, ad, bc, bd and cd), four three-way interactions (abc, acd, bcd and abd) and one four-way interaction (abcd). So, in many situations we may end up in large number of interactions and it is very rare to see three-way interaction in the experiments. As a result, higher order interactions have less impact.

As three-way interactions are uncommon, there is redundancy in full factorial designs. As a result, it is always preferable to use fractional-factorial design to take advantage of this redundancy. Because of resource constraint, time constraint with less number of experiments we should get for main effects and main interactions.

Fractional Factorial design (2^{k-q})

Fractional factorial designs are fractions of these main full factorial designs. We can have half fractional factorial design, if q=1. It means of half of full factorial; q=1 denotes one-fourth of full factorial even can have one-eighth of full factorial. Factor q aliased with high order interactions.so the number of experiments goes down. To identify critical parameter and to eliminate noise parameter.[14] This method used to study main effects of a large number of factors.

Table 7 a, b and c show the effect and interaction of independent factors such as (surfactant, agitation time and PH). The design is intended for 2^3 factors. If the formulator needs to investigate the effect of the fourth factor (d), which is polymer, in the given design Table 7. The design will then consist of 2^4 (2*2**2*2=16 experiments/runs) in case of full factorial design. Instead of running 16 runs using fractional factorial design, the formulator can study the interaction of four factors (a, b, c and d) in only eight runs i.e. (2^{4-1}) called Resolution IV design in the same design matrix.

Consider three order interactions (abc) as a D factor in the Table 7, for example a polymer. Following D as an independent factor, the second order interactions are AD, BD and CD. In the design Table 7, AD interactions resemble BC, BD interactions resemble AC and CD interactions resemble AB. It exists already within the design matrix. These fashion follows for three-way interactions too like BCD, ACD and ABD resemble like A, B and C in the design Table 7.

Instead of 16 experiments the fraction factorial design spews out only 8 experiment/runs. Where some of the factors are confounded as mentioned. In inference the design will not allow to differentiate all the two-way interaction like between AB against CD, AC against BD, BC against AD. The same fashion follows for three-way interactions. The main effects (A, B, C and D) or principle effects confounded with three-way interaction (BCD, ACD, ABD and ABC).

Therefore, all the two-way interactions confounded with two-way interactions and all main factors/effects confounded or aliased with the three-way interactions.

Screening design

A screening design is chosen to minimize the number of test runs. The minimum number of test runs allows for the rapid identification of factors that significantly affect the response. Factors that are found to be significant are then studied in more detail in subsequent tests. The most popular screening designs with a low number of test runs are Taguchi and Plackett Burman designs.

Taguchi Method

Genichi Taguchi, a Japan born is the pioneer of Taguchi method which is typically a robust design. Robustness is a condition of less sensitiveness to the external factors and achieves the targeted value and gives the desirable performance. Emphasize on robustness of the Taguchi design, brought his concept in the domain of design of experiment.[15]

Taguchi used the mathematical concept that is the orthogonal arrays. The execution of experiment by keeping robustness in consideration randomness was studied by the adopting the concept of orthogonal array.[16] The idea of orthogonal array will reduce the size of experimentation by avoiding numerous higher-level interactions. Robustness was achieved by concentrating on Signal by Noise ratio. Noise is interference due to external factors which may deteriorate the performance of the method. Hence for better robustness noise factor need to be minimized and signal factor need to be maximized.[17]

Control factors and noise factors

There are two main types of factors in a Taguchi design: the control factors and the noise factors. A control factor is a process or design parameter that can be controlled. For example, raw materials or temperature can be controlled.

Noise factors are those parameters that are difficult or expensive to control during manufacturing or method development. Examples of noise factors are deteriorated ingredients, wear and tear of instrument

Orthogonal array

The factors impacting the process and the levels at which they should be varied are organized using orthogonal arrays. The Taguchi approach tests pairs of possibilities rather of needing to test all conceivable combinations, as with the factorial design.[18]

The orthogonal arrays have the following unique characteristics.

Each variable's column in Table 8 has a unique set of level settings. The same amounts of levels occur at each level. Levels 1, 2 and 4 are present for each column of the L8 array four times.

All possible permutations of level settings for any given pair of columns (i.e. variables).

There are eight combinations of levels for the L7 orthogonal array and each combination only appears once. The equalizing feature of orthogonal arrays is the collective name for the first and second

Table 6: Order of interaction for full factorial design.

Number of factors	Main effects	Order of Interactions								
		2	3	4	5	6	7	8	9	10
2 (a,b)	2 (a,b)	1(ab)								
3	3	3	1							
4	4	6	4	1						
5	5	10	10	5	1					
6	6	15	20	15	6	1				
7	7	21	35	35	21	7	1			
8	8	28	56	70	56	28	8	1		
9	9	36	84	126	126	84	36	9	1	
10	10	45	120	210	252	210	120	45	10	1

qualities. All the levels of all the variables are used for conducting the experiments.

Because every column in the Table 8 is orthogonal to every other column, the order in which the experiments are conducted cannot be altered.[19]

Advantages

The Taguchi technique has the benefit of emphasizing mean performance characteristic values close to the goal value rather than values within specified specification boundaries, which raises the caliber of the final product. Taguchi's approach to experimental design is user-friendly and can be applied to a wide range of critical applications, making it an effective yet uncomplicated tool. This approach can be employed to quickly reduce the size of a research program or to identify issues in a production process from existing data. The Taguchi method also makes it possible to analyze a lot of different parameters without having to do a ton of experiments. For instance, if we had 7 variables in a process with 2 states each, it would take 128 experiments to get all the variables tested. But with Taguchi, we only need to do 8, which is mere 3% of what we need. That way, we can observe` which parameters have the most impact on the performance indicator, so we can do more experiments on them and ignore the ones that don't.[20]

Disadvantages

The main drawback is that the result obtained is only relative and does not provide an exact indication of which parameter has the greatest impact on the PIC value. Also, since the orthogonal array does not test all possible combinations of variables, it is not necessary to use this method with all the relationships between all the variables being tested. The Taguchi methodology has been criticised in the literature because it is difficult to account for the interactions between the parameters. Since the Taguchi methods focus on designing quality in and not correcting for low quality, they tend to be most effective at the early stages of the process development. Once design variables are defined, experimental design may become less cost effective.

Plackett-Burman design (PB)

The method was developed by RL Plackett and JP Burman in the year 1946. In this design only main effects of a method or process are taken in to consideration and all the interaction effects of the factors are neglected.[21] The design is mainly used to study K=N-1 variables where N is a multiples of 4. K and N are number of factors and number of experiments respectively. The design uses standard orthogonal arrays. If N is the power of 2, PB design is identical to 2k-pdesign. The PB design are majorly used to study

Table 7: 2^{4-1} Fractional factorial design matrix.

		Factors			Interaction			
		BCD	ACD	ABD	CD	BD	AD	D
Runs	tc	A	B	C	AB	AC	BC	ABC
1	(1)	-1	-1	-1	+1	+1	+1	-1
2	a	+1	-1	-1	-1	-1	+1	+1
3	b	-1	+1	-1	-1	+1	-1	+1
4	ab	+1	+1	-1	+1	-1	-1	-1
5	c	-1	-1	+1	+1	-1	-1	+1
6	ac	+1	-1	+1	-1	+1	-1	-1
7	bc	-1	+1	+1	-1	-1	+1	-1
8	abc	+1	+1	+1	+1	+1	+1	+1

Table 8: Seven-Factor Eight-Run Taguchi Design Matrix for Screening of Method Variables and Process Parameters at their Respect Low and High Levels.[11,13]

Run	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
1	+1	+1	-1	+1	-1	+1	+1
2	+1	+1	+1	-1	+1	+1	+1
3	+1	-1	-1	-1	-1	-1	+1
4	-1	-1	+1	-1	-1	+1	-1
5	-1	+1	-1	-1	+1	-1	-1
6	-1	+1	+1	+1	-1	-1	-1
7	+1	-1	+1	+1	+1	-1	+1
8	-1	-1	-1	+1	+1	+1	-1

Table 9: Plackett-Burman design for 11 factors with 12 runs.[25]

Runs	Pattern	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11
1	++++++++++	+1	+1	+1	+1	+1	+1	+1	+1	+1	+1	+1
2	-+-+++---+-	-1	+1	-1	+1	+1	+1	-1	-1	-1	+1	-1
3	--+-+++---+	-1	-1	+1	-1	+1	+1	+1	-1	-1	-1	+1
4	+--+-+++---	+1	-1	-1	+1	-1	+1	+1	+1	-1	-1	-1
5	-+--+-+++--	-1	+1	-1	-1	+1	-1	+1	+1	+1	-1	-1
6	--+--+-+++-	-1	-1	+1	-1	-1	+1	-1	+1	+1	+1	-1
7	---+--+-+++	-1	-1	-1	+1	-1	-1	+1	-1	+1	+1	+1
8	+---+--+-++	+1	-1	-1	-1	+1	-1	-1	+1	-1	+1	+1
9	++---+--+-+	+1	+1	-1	-1	-1	+1	-1	-1	+1	-1	+1
10	+++---+--+-	+1	+1	+1	-1	-1	-1	+1	-1	-1	+1	-1
11	-+++---+--+	-1	+1	+1	+1	-1	-1	-1	+1	-1	-1	+1
12	+-+++---+--	+1	-1	+1	+1	+1	-1	-1	-1	+1	-1	-1

the number of experiments N=12, 20, 24, 36 etc. As PB can't be represented as cubes they are called non geometric designs.

If we have a study of four factors, then four experiments will be relatively insufficient, hence by running a PB design one can have eight experiments with seven factors.

This implies that three of the aforementioned factors will serve as placeholders and hold no chemical significance. Nevertheless, it has been discovered that the perceived impact of these placeholders can be utilized to approximate the stochastic measurement errors.[22] The inclusion of additional placeholders leads to a more precise estimation of such errors, hence it is not unusual for researchers to employ a larger PB design than strictly required, thereby obtaining superior quality data on the significance of each genuine factor. The sample design was presented in Table 9. The Plackett-Burman design also employs a two-level approach, wherein high and low levels are assigned to trial experiments in a cyclical manner.[23]

Advantages

Efficient Screening

One of the primary advantages of the Plackett-Burman design is its efficiency in screening a large number of factors (variables) with a relatively small number of experimental runs. This can significantly reduce the time, cost and resources required for experimentation.

Identifying Key Factors

This design helps identify the most significant factors that have an impact on the response variable. By conducting a limited number of experiments, researchers can quickly pinpoint which factors are worth further investigation, saving time and resources in the long run.[24]

Simple and Easy to Implement

The Plackett-Burman design is relatively easy to understand and implement, even for those without extensive statistical expertise. It doesn't require complex calculations or specialized software.

Reduction of Experimental Error

By using a fractional factorial design, the Plackett-Burman design minimizes experimental error and noise, increasing the reliability of the results obtained.

Applicability to Various Fields

This design is versatile and can be applied in various fields, including pharmaceuticals, manufacturing, agriculture and more. It's particularly useful when there are limited resources available for experimentation.

Limitations

Only Identifies Main Effects

Plackett-Burman designs are limited to identifying main effects, which means they may not capture interactions between factors. If interactions are suspected to be significant, a more extensive experimental design may be needed.

Assumes Linearity

The design assumes that the relationships between factors and the response variable are linear. If the actual relationships are nonlinear, the results may not accurately represent the system's behavior.

No Information on Optimal Settings

Plackett-Burman designs focus on identifying important factors but do not provide information on the optimal settings for these factors. Further optimization experiments are usually required to determine the best conditions.[26]

Limited Resolution

While the design is efficient for screening, it has limited resolution, which means it may not distinguish between factors with similar effects on the response variable. Additional experiments may be needed to refine the understanding of these factors.

In summary, the Plackett-Burman design is a valuable tool for efficiently screening a large number of factors and identifying the most important ones. It is particularly useful for initial investigations and can save time and resources in the early stages of research or process development.[27] However, researchers should be aware of its limitations and consider more advanced experimental designs when interactions and optimal settings are critical for their objectives.

DISCUSSION

The existing review on Design of Experiments (DoE) extensively covers various advanced applications, such as screening and optimization, focusing on methodologies like full factorial, Taguchi and Plackett-Burman designs. These studies highlight their effectiveness in identifying critical factors and improving processes. However, this review adds value by emphasizing the foundational aspects of DoE, including the basic concepts of factors, levels and response variables, as well as the importance of proper experimental design and statistical analysis. By focusing on the fundamentals, this review ensures a deeper understanding of DoE's core principles and offers practical insights that reinforce its significance across various fields of research.

CONCLUSION

This comprehensive review on the appliance of Design of Experiments (DOE) in the context of screening and optimization experiments underscores the invaluable role this methodology plays in advancing research, product development and process optimization across a myriad of fields. By systematically planning, conducting and analyzing experiments, DOE offers a structured approach to unravel complex relationships between variables, ultimately leading to informed decision-making and improved outcomes.

Throughout this review, we have explored the fundamental principles of DOE, from the definition of factors and response variables to the selection of appropriate experimental designs. We have examined various types of designs, including full factorial, fractional factorial, Plackett-Burman designs elucidating their unique strengths and applications. Outstandingly, this review has emphasized the practical aspects of DOE, from the critical phases of experimental planning to the statistical analysis of results. It has also highlighted the growing integration of computational tools and software, making DOE more accessible and efficient for practitioners.

DOE has revolutionized industries such as manufacturing, pharmaceuticals and engineering by saving resources, time and, most significantly, by enhancing product quality and process efficiency. In today's increasingly competitive and data-driven world, the knowledge and application of Design of Experiments are more critical than ever. This review serves as a valuable resource for researchers, practitioners and decision-makers alike, offering insights into DOE's adaptability, practical implementation and its potential to drive innovation and excellence in experimentation and decision-making processes. As we move forward, it is clear that DOE will continue to be a cornerstone of scientific and industrial progress, driving us towards more efficient and effective experimentation and optimization.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

ABBREVIATIONS

QbD: Quality by design; **BBD:** Box-Behnken design; **Opt:** Optimized; **DoE:** Design of experiment; **PIC:** Polymorphic Information Content; **PBD:** Plackett-Burman design.

SUMMARY

Design of Experiments (DOE) is a systematic approach widely used across various fields to plan, execute and analyze experiments efficiently. This review provides an in-depth look at DOE's application in screening and optimization experiments. Screening experiments identify significant factors influencing a response, while optimization experiments refine these factors to achieve the best outcomes. The review covers fundamental DOE concepts such as factors, levels and response variables and discusses popular screening designs like full factorial, Taguchi and Plackett-Burman, highlighting their pros and cons. Practical aspects of DOE, including proper planning, statistical analysis, design selection, sample size determination and data analysis techniques are thoroughly explored. The integration of computer-aided tools and software in DOE is also examined, showcasing its role in enhancing efficiency and accessibility. The review emphasizes DOE's impact on saving resources and time and its potential for improving product quality and process efficiency, making it a valuable resource for researchers and practitioners aiming to optimize their experimental processes.

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