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APPLICATIONS OF FACTOR ANALYSIS AND RESPONSE SURFACE METHODOLOGY IN CHEMICAL PROCESS OPTIMIZATION PROBLEMS

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Article listory:	optimize processes in chemical industries.
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Accepted 24 January 2024	Design of Experiments (DoE) is widely used for the for the implementation of Quality by Design (QbD) in both research and industry. In QbD, understanding the product
Keywords:	and the process is the key factor in ensuring the quality of the end product (Politis et al., 2017).
Design of Experiments; Complete Factorial Design; Response Surface Methodology.	Method: An assessment was made of the best method for creating mathematical models using Pareto graphs, factor graphs, contour graphs, response surface graphs and analysis of variance.
\bigcirc	Results and Conclusion: In both case studies, the statistical tools proved to be suitable for analyzing the processes and were able to find the optimum process factors to guarantee the best possible response variable.
PREREGISTERED OPEN DATA OPEN MATERIALS	Originality/Value: Design of Experiments (DoE) is the main component of the statistical toolbox to deploy Quality by Design in both research and industrial settings.
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APLICAÇÕES DA ANÁLISE FATORIAL E DA METODOLOGIA DE SUPERFÍCIE DE RESPOSTA EM PROBLEMAS DE OTIMIZAÇÃO DE PROCESSOS QUÍMICOS.

RESUMO

Objetivo: Este trabalho tem como objetivo mostrar duas aplicações do Design de Experimentos para otimizar processos em indústrias químicas.

Referencial Teórico: Entre as várias abordagens de modelagem matemática, o Design de Experimentos (DoE) é amplamente usado para a implementação do Quality by Design (QbD) tanto na pesquisa quanto no setor para a implementação do Quality by Design (QbD) tanto na pesquisa quanto no setor. No QbD, a compreensão do produto e do processo é o principal fator para garantir a qualidade do produto final (Politis et al., 2017).

Método: Foi realizada uma avaliação do melhor método para a criação de modelos matemáticos usando gráficos de Pareto, gráficos de fatores, gráficos de contorno, gráficos de superfície de resposta e análise de variância.

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Resultados e Conclusão: Em ambos os estudos de caso, as ferramentas estatísticas se mostraram adequadas para analisar os processos e foram capazes de encontrar os fatores ideais do processo para garantir a melhor variável de resposta possível.

Originalidade/Valor: O Design of Experiments (DoE) é o principal componente da caixa de ferramentas estatísticas para implementar o Quality by Design tanto em ambientes de investigação como industriais.

Palavras-chave: Projeto de Experimentos, Projeto Fatorial Completo, Metodologia de Superfície de Resposta.

APLICACIONES DEL ANÁLISIS FACTORIAL Y LA METODOLOGÍA DE SUPERFICIE DE RESPUESTA A PROBLEMAS DE OPTIMIZACIÓN DE PROCESOS QUÍMICOS

RESUMEN

Propósito: El objetivo de este artículo es mostrar dos aplicaciones del Diseño de Experimentos para optimizar procesos en la industria química.

Marco Teórico: Entre los diversos enfoques de modelado matemático, el Diseño de Experimentos (DoE) se utiliza ampliamente para la implementación de la Calidad por Diseño (QbD) tanto en la investigación como en la industria. En QbD, la comprensión del producto y del proceso es el factor clave para garantizar la calidad del producto final (Politis et al., 2017).

Metodo: Se evaluó el mejor método para crear modelos matemáticos utilizando gráficos de Pareto, gráficos factoriales, gráficos de contorno, gráficos de superficie de respuesta y análisis de varianza.

Resultados y conclusiones: En ambos casos, las herramientas estadísticas resultaron adecuadas para analizar los procesos y permitieron encontrar los factores de proceso idóneos para garantizar la mejor variable de respuesta posible.

Originalidad/Valor: El Diseño de Experimentos (DoE) es el principal componente de la caja de herramientas estadísticas para desplegar la Calidad por Diseño tanto en entornos de investigación como industriales.

Palabras clave: Diseño de Experimentos, Diseño Factorial Completo, Metodología de Superficie de Respuesta.

INTRODUCTION

Among various mathematical modeling approaches, Design of Experiments (DoE) is extensively used for the implementation of Quality by Design QbD in both research and industrial settings. In QbD, product and process understanding is the key enabler of assuring quality in the final product. Design of Experiments (DoE) is the main component of the statistical toolbox to deploy Quality by Design in both research and industrial settings. Fisher practically highlighted the need to consider statistical analysis during the planning stages of research rather than at the final phases of experimentation. As he emphasized in his famous quote: "to consult the statistician after an experiment is finished is often merely to ask him to conduct a post mortem examination (Politis et al., 2017).

Determining a process improvement is typically complex due to variations in customer demand and technological advances. Generally, several responses must be considered in order to achieve an overall process improvement (Antonio et al., 2023)

In the past decade or so, DoE has gained increasing importance in the reduction of variability in core processes, whereby consistent product quality can be achieved.

Moreover, companies striving for a six-sigma approach to achieving quality treats DOE as the key player (Antony, 2002).

Design of experiments (DoE) is one method that has proven to be very efficient in distinguishing major and minor contribution of factors on product studied. The purpose of design of experiments is to discover the critical variables, which influence the final product, their effects on variability and their respective settings. A design of experiments is the most economical and most accurate method for performing process optimization. A designed experiment will accelerate the learning of the interrelationships of the process variables, determine what variables are critical to the process and determine at what levels these variables are critical to the process (Rocak et al., 2002).

The statistically governed design of experiments (DoE) schemes used for physical experiments have been extensively used for deterministic computer experiments as well, but they are not necessarily optimal (Dersjö & Olsson, 2012).

This paper examines two applications of Design of Experiments for process optimization in the chemical industry.

LITERATURE REVIEW

Design of experiments (DoE) is a technique for defining which data should be collected in a given experiment. This technique is ideal for studying the effect of a set of various factors on a response variable of interest. The design of experiments carries out analyses to promote better operational performance and, consequently, a reduction in costs (Almeida E Silva & Okimoto, 2012). In order to improve industrial quality, productivity, final product performance, operating costs, among other characteristics, companies carry out various experiments to find the optimum levels of the parameters that regulate their manufacturing processes. Some of the problems encountered when carrying out tests is the need to simultaneously study the effect of factors at different levels of regulation. In this case, the number of tests required for experiments increases. This makes industrial experiments economically unviable, since the costs and time involved are high. Such problems can be circumvented when experiments are planned and analyzed using statistical methods and techniques. Among the various types of techniques are Full Factorial Design, Fractional Factorial Design, Response Surface Methodology and Taguchi Experiments (Coleman & Montgomery, 1995; Galdamez & Carpinetti, 2004; Montgomery, 2017).

Factorial design is a useful analytical strategy and its application lies in the selection of the most relevant variables in a given analytical of a given analytical system. After this screening process of the most significant variables, experiments are carried out which allow refinement and a better understanding of the system under study. In a laboratory study, the factorial experiment can be used to analyze differences in the yields of different varieties, as well as the different levels of function of a microorganism, for example. A model in each combination at all levels of factors are applied. From this perspective, understanding and designing the statistical control of all the experimental units in a sample leads to excellence in the quality of the goods and services processes of the final product final product to be desired (Selvamuthu & Das, 2018; Vicentini et al., 2011).

Response surface methodology is a collection of statistical and mathematical techniques useful for developing, improving and optimizing processes. It also has important applications in the planning, development and formulation of new products, and improving existing designs and products. The most extensive application of RSM is in the industrial field, particularly in situations where several variables come into play that potentially influence some measure of performance or quality characteristic of a product or process. of a product or process. This measure of performance or quality characteristic is called response(Myers, R.H. and Montgomery, 1995). Response surface methodology (RSM) is a collection of statistical design and numerical optimization techniques used to optimize processes and product designs. The original work in this area dates from the 1950s and has been widely used, especially in the chemical and process industries. The last 15 years have seen the widespread application of RSM and many new developments (Myers et al., 2004). Response surface methodology is a statistical technique used for modeling and analyzing modeling and analysis of problems in which the response variable is influenced by several factors, with the aim of optimizing this response (Comparini et al., 2009).

RESEARCH METHOD

This work can be classified as applied research, as it aims to provide improvements in the current literature, with normative empirical objectives, aiming at the development of policies and strategies that improve the current situation (Araujo et al., 2021; H. de O. G. da Silva et al., 2021; Will M. Bertrand & Fransoo, 2002). The approach to the problem is quantitative, as is the modeling and simulation research method. The research stages were carried out following the sequence shown in Figure 1.



Source: Authors (2024)

Case 1

The case study below is an optimization study carried out by the first author of this article for an undergraduate student at the State University of Rio de Janeiro, in Resende (RJ), where the aforementioned student carries out an internship in a Chemical Industry in the Southern Region of the State of Rio de Janeiro and works with a chemical process that uses these three factors studied, among these levels, and Table 1 shows the values that were analyzed using a Full Factorial Experiment carried out in Minitab 19 Software. The factors are not coded because, as the values are in the same order of magnitude, there is no need for this.

Temperature	Concentration	Catalyst
(oC)	(g/L)	Catalyst
160	20	А
180	20	А
160	40	А
180	40	А
160	20	В
180	20	В
160	40	В
180	40	В
160	20	А
180	20	А
160	40	А
180	40	А
160	20	В
180	20	В
160	40	В
180	40	В

Table 1 - Temperature, Concentration and Catalyst Values for the Factorial Experiment

Source: Authors (2024)

Case 2

The problem described (Silva et al., 2008) evaluates the influence of the amount of nitrogen, phosphorus and Brix levels on the yield and productivity of alcoholic fermentation. The methodology used was factorial design and response surface analysis. The aim of this study is to redo one of the analyses, more specifically the Productivity curve as a function of the amount of Nitrogen and Phosphorus to show the importance of the statistical technique used for modeling and analyzing problems in which the response variable is influenced by various factors, with the aim of optimizing this response. Table 2 shows the uncoded factorial planning matrix of the amounts of Nitrogen and Phosphorus with the response productivity of fermented alcohol, ready to be analyzed in the Minitab 19 software. This statistical technique adjusts empirical models to the experimental data obtained in relation to the experimental design and one of its advantages is that it can work with the possibility of moving in the direction of the optimum region and obtaining optimum values for each variable studied (Bezerra et al., 2008).

productivity of fermented account						
Nitrogen	Phosphorus	Productivity (g L-1h-1)				
(5)	(5)	5.00				
0.5	0.002	3.09				
0.6	0.002	5.19				
0.3	0.05	6.21				
0.6	0.05	6.23				
0.1977	0.026	5.31				
0.7023	0.026	5.09				
0.45	-0.014368	5.64				
0.45	0.066368	6.63				
0.45	0.026	5.13				
0.45	0.026	5.6				
0.45	0.026	6.39				
0.45	0.026	6.43				
0.45	0.026	6.42				
Source: Authors (2024)						

Table 2 – Uncoded Factorial Planning Matrix of the amounts of nitrogen and phosphorus with the Response productivity of fermented alcohol

RESULTS AND DISCUSSION

Case 1

Using factorial experimental design, the interactions of the possible parameters influencing treatment efficiency and the individual factors can be evaluated with a limited number of planned experiments, which makes the realization of the process more economically viable (Tahri Joutey et al., 2015).

The first step is to analyze which of the three factors presented, each with 2 levels (low and high), are important for obtaining the highest possible yield. To do this, we carried out a

Full Factorial Experiment with 3 factors and 2 levels with 1 replicate, where we obtained a Pareto Graph as shown in Figure-2 and an Analysis of Variance (ANOVA) as shown in Table 1, both with a 95% confidence level to show the importance of the factors. The t-critical value given by Minitab 19 software was 2.31.



Source: Authors (2024)

The result clearly shows that the effects of Temperature (A), the effect of the Temperature and Catalyst Interaction (AC) and the effect of Concentration (B) are the significant ones for the Yield response variable as they were above the critical t of 2.31. This can also be seen in Table 3, which shows the Analysis of Variance where only these Factors have a p-Value of less than 0.05 (5%): Temperature (0.0), Temperature and Catalyst Interaction (0.0) and Concentration (0.08). In Factorial Planning, when one factor interacts with another, the main factor is not analyzed, so only the Interaction of Temperature with Catalyst (AC) and Concentration (B) will be analyzed, leaving Temperature (A) out because it interacts with another factor. The Adjusted R^2 reached a value of 95.5%, considered optimal, meaning that the dependent variable Yield is explained in this percentage by the significant independent variables Temperature (A), Temperature and catalyst interaction (AC) and Concentration (B).

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Source	GL	SQ (Aj.)	QM (Aj.)	F Value	P-Value
Model	7	2635,00	376,43	47,05	0,000
Linear	3	2225,00	741,67	92,71	0,000
Temperature	1	2116,00	2116,00	264,50	0,000
Concentration	1	100,00	100,00	12,50	0,008
Catalyst	1	9,00	9,00	1,13	0,320
2-factor interactions	3	409,00	136,33	17,04	0,001
Temperature*Concentration	1	9,00	9,00	1,13	0,320
Temperature*Catalyst	1	400,00	400,00	50,00	0,000
Concentration*Catalyst	1	0,00	0,00	0,00	1,000
3-factor interactions	1	1,00	1,00	0,13	0,733
Temperature*Concentration*Catalyst	1	1,00	1,00	0,13	0,733
Error	8	64,00	8,00		
Total	15	2699,00			

Source: Authors (2024)

In order to evaluate the best levels for the interaction between the Temperature and Catalyst (AC) factors, a Factor Graph of the interaction between these Factors was carried out, which is shown in Figure -3. It is clear that the search is for the best possible Yield (Response Variable), which occurs at 180°C using Catalyst B, producing a Yield of 81.5. At the lower temperature of 160oC Catalyst A is more effective while at the higher temperature of 180°C Catalyst B is more effective. The Adjusted R^2 reached a value of 35.88%, considered average, meaning that the dependent variable Productivity is explained in this percentage by the significant independent variable Phosphorus (B). As there is only one independent variable, although the model is well adjusted, there is a loss of robustness because of this. The adjusted R-squared or modified R² determines the extent of the variance of the dependent variable that can be explained by the independent variable. The specialty of adjusted R² is that it does not take into account the impact of all the independent variables, but only those that have an impact on the variation in the dependent variable. The higher the adjusted R², the better the regression equation, since it implies that the independent variable chosen to determine the dependent variable can explain the variation in the dependent variable. At approximately 168°C the two lines meet and this means that at this temperature the two catalysts produce the same yield.



Figure 3 – Factorial Graph of the Interaction between Temperature and Catalyst

Source: Authors (2024)

Next, a factorial graph is made for the main effect Concentration (B), which appears in Figure 4. It is clear that the maximum yield occurs when the concentration is equal to 20 g/L and the minimum yield value occurs at a concentration of 40 g/L. Now we can carry out the experiment (bench) or the process (chemical reactor) by setting the factors at the correct levels to obtain the best possible yield. The graph has an important function as it clearly shows that an increase in Concentration produces a linear decrease in the response variable Yield.



Source: Authors (2024)

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Case 2

The Response Surface Methodology is the appropriate statistical technique for modeling an experiment in which we imagine that there is a curve and an optimum point, which can be the point of maximum. The first-degree polynomial model is to use a factorial experiment or a fractional factorial design. This is sufficient to determine which explanatory variables affect the response variable(s) of interest. When it is suspected that only significant explanatory variables remain, a more complicated design, such as a central composite design, can be implemented to estimate a second-degree polynomial model, which is still only an approximation at best. However, the second-degree model can be used to optimize (maximize, minimize or achieve a specific goal for) the response variable(s) of interest. (Chelladurai et al., 2020; Comparini et al., 2009).



Source: Authors (2024)

The result clearly shows that the effect of Phosphorus (B) is the only significant one for the Productivity response variable, since it was higher than the critical t-value of 2.365. This can also be seen in Table 4, which shows the Analysis of Variance where only this Factor has a p-value of less than 0.05 (5%): Phosphorus (0.037).

Sampaio, N. A. de S., Miranda Júnior, J. E., de Almeida, M. da G. D., de Abreu, L. D., Cardoso, R. P. (2024) Applications of Factor Analysis and Response Surface Methodology in Chemical Process Optimization Problems

Source	GL	SQ (Aj.)	QM (Aj.)	F Value	P-Value
Model	5	2.69551	0.53910	2.34	0.149
Linear	2	1.52145	0.76072	3.31	0.098
Nitrogen	1	0.00647	0.00647	0.03	0.872
Phosphorus	1	1.51497	1.51497	6.58	0.037
Square	2	1.17246	0.58623	2.55	0.147
Nitrogen*Nitrogen	1	1.00969	1.00969	4.39	0.074
Phosphorus*Phosphorus	1	0.02023	0.02023	0.09	0.775
Interaction with 2 Factors	1	0.00160	0.00160	0.01	0.936
Nitrogen*Phosphorus	1	0.00160	0.00160	0.01	0.936
Error	7	1.61057	0.23008		
Lack of fit	3	0.18045	0.06015	0.17	0.913
Pure error	4	1.43012	0.35753	*	*
Total	12	4.30608			

Table 4 - Analysis of Variance Table

Source: Authors (2024)

As the lack of fit gave a pvalue greater than 0.05 (5%), more specifically 0.913 (91.3%) the lack of fit is not significant and the model is well adjusted. Figure 6 shows the graph of the effect of Phosphorus on Productivity. It is easy to see that the higher the concentration of Phosphorus, the higher the Productivity value.





This information can also be seen in Figure 7 (Contour Graph for Productivity) and Figure 8 (Surface Graph for Productivity). In the first (Contour Graph) the point of highest

Productivity (around 6.5 gL-1h-1) occurs with Phosphorus above 0.06 g and the influence of Nitrogen is small (0.3g to 0.6g of Nitrogen reaches the Optimum Range. In the second (Surface Graph) it is easy to see that the Nitrogen axis is at the same height and the Phosphorus axis has an increasing slope, directly proportional to the increase in Phosphorus, only confirming that it is the Significant Factor.



Source: Authors (2024)



Figure 8 – Productivity Surface Graph

Source: Authors (2024)

CONCLUSION

This work was carried out with the aim of showing the importance of Design of Experiments for applications in the chemical area. In case study 1 we used the Full Factorial methodology to study the Yield of a chemical reaction as a function of its factors and in case study 2 we used the Response Surface methodology to analyze the Productivity of an Alcoholic Fermentation Process also as a function of its factors. In both cases the Statistical Tools worked perfectly and it was possible to show who the significant factors were and the optimum range for both, so that in a laboratory or process situation it is simply a matter of choosing the optimum range of factors in order to achieve the best results for the dependent variable. A suggestion for future work is to use these tools in other case studies and define which of them is most effective in certain problem situations.

REFERENCES

Almeida E Silva, C. M., & Okimoto, M. L. R. L. (2012). Design of experiment with emphasis on intuitive use. *Work*, *41*(SUPPL.1), 1100–1107. https://doi.org/10.3233/WOR-2012-0288-1100

Antonio, N., Sampaio, D. S., Salvador, J., Glenio, J., C, M. D. B., D, C. P. D. C., E, F. M. G., César, L., Motta, F., & G, M. B. S. (2023). *Multiple Response Optimization: Comparative Analysis Between Models Obtained by Ordinary Least Method and Genetic Programming*. 1–23. https://doi.org/10.26668/businessreview/2023.v8i8.3131

Antony, J. (2002). Training for design of experiments using a catapult. *Quality and Reliability Engineering International*, *18*(1), 29–35. https://doi.org/10.1002/qre.444

Bezerra, M. A., Santelli, R. E., Oliveira, E. P., Villar, L. S., & Escaleira, L. A. (2008). Response surface methodology (RSM) as a tool for optimization in analytical chemistry. *Talanta*, 76(5), 965–977. https://doi.org/10.1016/j.talanta.2008.05.019

Chelladurai, S. J. S., Murugan, K., Ray, A. P., Upadhyaya, M., Narasimharaj, V., & Gnanasekaran, S. (2020). Optimization of process parameters using response surface methodology: A review. *Materials Today: Proceedings*, *37*(Part 2), 1301–1304. https://doi.org/10.1016/j.matpr.2020.06.466

Coleman, D. E., & Montgomery, D. C. (1995). A Systematic Approach to Planning for a Designed Industrial Experiment. *Technometrics*, *1*. https://doi.org/10.1080/00401706.1993.1 0484984

Comparini, A., Passos, G., Graziadei, H., Ferreira-Silva, P. H., & Louzada, F. (2009). Metodologia De Superfície De Resposta: Uma Introdução Nos Softwares Re Statistica. *São Carlos*, *1001*, 14. http://www.icmc.usp.br/CMS/Arquivos/arquivos_enviados/BIBLIOTECA_113_RT_376.pdf Dersjö, T., & Olsson, M. (2012). Efficient design of experiments for structural optimization using significance screening. *Structural and Multidisciplinary Optimization*, 45(2), 185–196. https://doi.org/10.1007/s00158-011-0677-0

Galdamez, E. V. C., & Carpinetti, L. C. R. (2004). Aplicação das técnicas de planejamento e análise de experimentos no processo de injeção plástica. *Gestão & Produção*, *11*(1), 121–134. https://doi.org/10.1590/s0104-530x2004000100011

Montgomery, D. C. (2017). Design and Analysis of Experiments. In Wiley (9°). Wiley.

Myers, R.H. and Montgomery, D. C. (1995). *Response Surface Methodology: Process and Product Optimization Using Designed Experiments*. John Wiley and Sons.

Myers, R. H., Montgomery, D. ., Vining, G. G., M. Borror, C., & Kowalski, S. M. (2004). Response Surface Methodology: A Retrospective and Literature Survey. *Journal of Quality Technology*, *36*. https://doi.org/10.1080/00224065.2004.11980252

Politis, S. N., Colombo, P., Colombo, G., & Rekkas, D. M. (2017). Design of experiments (DoE) in pharmaceutical development. *Drug Development and Industrial Pharmacy*, 43(6), 889–901. https://doi.org/10.1080/03639045.2017.1291672

Rocak, D., Kosec, M., & Degen, A. (2002). Ceramic suspension optimization using factorial design of experiments. *Journal of the European Ceramic Society*, 22(4), 391–395. https://doi.org/10.1016/S0955-2219(01)00309-0

Selvamuthu, D., & Das, D. (2018). Introduction to Statistical Methods, Design of Experiments and Statistical Quality Control (Textbook (SPRINGER) (ed.)).

Silva, J. A., Damasceno, B. P. G. D. L., Da Silva, F. L. H., Madruga, M. S., & De Santana, D. P. (2008). Application of the factorial design and response surface methodology for optimization of alcoholic fermentation. *Quimica Nova*, *31*(5), 1073–1077. https://doi.org/10.1590/s0100-40422008000500024

Tahri Joutey, N., Bahafid, W., Sayel, H., Maâtaoui, H., Errachidi, F., & El Ghachtouli, N. (2015). Use of Experimental Factorial Design for Optimization of Hexavalent Chromium Removal by a Bacterial Consortium: Soil Microcosm Bioremediation. *Soil and Sediment Contamination*, 24(2), 129–142. https://doi.org/10.1080/15320383.2014.922931

Vicentini, F. C., Figueiredo-Filho, L. C. S., Janegitz, B. C., Santiago, A., Pereira-Filho, E. R., & Fatibello-Filho, O. (2011). Planejamento fatorial e superfície de resposta: Otimizaç ão de um método voltamétrico para a determinação de Ag(I) empregando um eletrodo de pasta de nanotubos de carbono. *Quimica Nova*, *34*(5), 825–830.