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The optimal design of experiments (ODOE) as an alternative method for catalysts libraries optimization

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ABSTRACT

A comparative study was made between two optimization strategies for the development of heterogeneous catalytic materials. The evolutionary approach (EA), which is based on genetic algorithms (GA), is a well-proven stochastic strategy here used as a reference to evaluate our library optimization method (CLOM), which is based upon the optimal design of experiments (ODOE). This method was validated by means of two virtual models that correlate the performance and the formulation of a catalytic system. In order to build up the ODOE three criteria were considered: (1) D-Optimality's criterion, (2) a reduced set of 240 experiments and (3) a statistical model with at least two-parameter interactions. The sets of experiments proposed by the ODOEs were evaluated using the validation models and the results were used to fit the statistical models. The optimization of the fitted model was made by a traditional optimization technique (i.e. Levenberg–Marquard's) and the resulting optimal formulations were very close to the validation models with an error lesser than 3%. Also, a considerable reduction of the total number of experiments was achieved by means of ODOE and CLOM, i.e. a catalytic system with up to eight components needed 40% of the experiments required by the reference method.

1. Introduction

The combinatorial and high-throughput techniques have become an important tool to speed up the discovery of new materials and catalysts. Since the very first publication on combinatorial methods applied to materials development [1] the implementation of these technologies has evolved from an early euphoria to a rational maturity. However, the application of these methods to heterogeneous catalysts has taken almost 15 years [2–10]. In this respect, a recent publication was made by Maier et al. [8], who point out the importance of the preparation and evaluation conditions as well as the data analysis and management, but most of the previous reviews focused on high-throughput synthesis and screening devices, rather than catalysts library optimization methods (CLOM). More recently, Farrusseng [10] reviewed the methods of library design for improving the routes of discovery and optimization of new catalysts, with special emphasis on advanced methods and new knowledge. These methods focused on the development of empirical expressions for correlating the catalysts performance with some synthesis parameters. Also, Maier's [10] emphasize the methods of design of experiments (DoE), which agrees with Holena's idea [11] of dividing all the methods into two groups: (1) optimization methods that do not require gradient or second derivates to reach an optimum point (i.e., simplex method, simulated annealing, or genetic algorithms) [12–22] and (2) the methods based upon an analytical expression that might be built up from available experimental data, i.e., multi-regression analysis, statistical DoE and artificial neural networks (ANN). The success of the fitted model depends on the quality of data used for experimental design and on the chosen model. Thus, the present work considers the existence of one general approach that includes the two groups described above without excluding these methods by themselves. The main objective is to build up a strategy for looking for an optimal formulation of a specific catalytic system that promotes a feasible model. A successful example of the merge between GA and ANN. [23–28] is the capability of the former method to extend the search through the whole parameter space in a coherent way and the NN's ability to outline an accurate correlation between performance and synthesis parameters. However, due to the stochastic dependency of these methods the GA's predictions

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remain specific for the cases where few populations are studied. Additionally, if one considers bigger topologies, NN could be overfitted; which drives the search out of the real optimal zone. To confirm the accuracy an increase of the number of experiments is mandatory, which guarantees a broad coverage of the parameter space and it ensures the inclusion of different promising zones [29]. Besides, the NN model must be continuously improved with new experimental results and this implies that previous experiments that were discarded could be reevaluated with the enhanced NN, in order to confirm unattractive zones or to reconsider them into the search [30]. In any case, this stochastic character affects the whole confidence on these methods. Thus, a formal design of experiments (DOE) was applied by Cawse et al. for the development of a tri-metallic catalyst used for carbonylation of phenol [31] and these studies [32] were implemented in commercial software [33]. Also, Hanefeld [34] used a multi-step DOE approach to optimize the catalytic hydrogenation of acylated cyanohydrins to *N*-acyl β-amino alcohols, which required only 70-experiments out of 2000 possible combinations of the categorical parameter levels. The multi-step DOE approach consisted of three stages, one focuses on an ODOE followed by two others, where the traditional full factorial DOEs were applied. This method allows discarding irrelevant parameters along subsequent optimization steps. The success of using sequential application of small DOEs, instead of a big one, lies in the remarkable feature of avoiding the evaluation of futile parameters that might be identified in previous stages.

Recently, HT synthesis and evaluation systems based on DOEs have been used to optimize few factors in the catalysts formulation and reaction conditions [9,35,36]. DOEs are able to manage both method stages but in this case the uncertainty is lowered by the optimal location of the experimental determinations. However, the application of these procedures to more than five variables is limited due to the number of experiments required for a specific case. Moreover, when the constrained parameter spaces are researched as it occurs in the case of mixture designs; and if the experimental planning considers combinations of continuous and discrete variables, as expected in catalysts research, the optimal designs of experiments (ODOEs) could be successfully implemented [37,38].

Therefore, in this work we explore a proper implementation of ODOEs to drive the search of optimal catalysts formulation and this approach is validated on two hypothetical catalytic systems. We compared the optimal results to those obtained by means of a well-proven strategy based on GA, [12,14] and also with respect to a trained neural network. The results might indicate that an improved strategy could be implemented by the adequate use of ODOEs in the search of optimal catalysts formulation, with a low number of experimental points, which is required even when combinations of continuous and discrete variables are sought.

2. Experimental

There are three consecutive stages of a global strategy in combinatorial catalysis: (1) A mapping is devoted to the study of a huge number of elements to be formulated, thus a search for synergetic effects that might be non-identified previously. (2) A screening stage is directed toward the identification of the small regions that have a well-defined parameter space, where the parameters that cause lower effects are discarded. (3) An optimization stage is directed to experimental planning that is carried out to refine and optimize the properties of catalytic materials and the optimal operation conditions; in this stage the small and narrow parameter spaces are typical [39]. Thus, the traditional factorial DOEs are suitable for the screening stage directed toward the estimation of the effect parameter. For optimization the Central composite or Box-Behnken designs and the typical response surface design are better suited for ensuring a response prediction.

Considering that the main purpose of DOEs is to collect the information by running a minimum number of experiments, a very important feature of this approach is the ability to identify the effect of the interactions among different variables. Hence, the screening of parameters with low effect on the response variable could be achieved early in the research. The correct application of this strategy narrows down the higher dimensional parameter space, which allows to build up consecutive DOEs to optimize the catalyst formulation or operational conditions. Furthermore, DOEs can be adapted to the needs of high-throughput experimentation (HTE) [35,36], thus consecutive and properly planed DOEs could be adapted to the available synthesis or evaluation wells.

2.1. Predictive model for a mixture design

In traditional DOEs implementation, i.e., the factorial design, some parameters are varied independently from one another, which results in an orthogonal design, that is the absence of a correlation among these factors. This guarantees independent estimations of the effect of each factor on the response [40]. However, HT catalysis research commonly deals with mixtures of components, and a single component contribution depends on each other. In this case, independent estimations of factor effects are impossible, limiting application of traditional DOEs.

Classical DOE proposes a full or fractional factorial design with multiple levels for factors to drive the search. These designs allow estimation of interaction effects and the identification of the optimal combination of factor levels. Then the model to be fitted is

$$E(y) = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i<j=1}^{k} \beta_{ij} X_i X_j \quad (1)$$

where all main effects and two-factor interactions are included [41]. With this model a quick discarding of low effect factors is achieved, suitable for the screening stage. But if the objective is to optimize formulation, a response surface design, such as central composite or Box-Behnken, is commonly used. The approximated relationship obtained between response y and k quantitative factors is optimized by traditional methods, Eq. (2).

$$E(y) = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i<j=1}^{k} \beta_{ij} X_i X_j + \sum_{i=1}^{k} \beta_{ii} X_i^2 \quad (2)$$

Considering the optimization of a typical catalyst formulation, the configured optimization problem is based on a mixture of oxides, the mixture constrain must be observed, Eq. (3),

$$\sum_{i=1}^{k} X_i = 1 \quad (3)$$

and the independent term in Eqs. (1) and (2), β_0, becomes null, due response is not expected in the absence of catalyst. Simplex designs are used to study the effects of mixture components on the response variable. Eqs. (4) and (5) corresponds to mixture model for Eqs. (1) and (2). The Eq. (6) shows the Sheffe model for a triple interaction among components, applied to avoid even-powered terms that are not estimable, i.e. $x_1{}^* x_1{}^* x_2$.

$$\text{Linear}: \quad y = \sum_{i=1}^{n} \beta_i x_i \quad (4)$$

$$\text{Quadratic}: \quad y = \sum_{i=1}^{n} \beta_i x_i + \sum_{i=1}^{n} \sum_{i<j}^{n} \beta_{ij} x_i x_j \quad (5)$$

$$\text{Cubic}: \quad y = \sum_{i=1}^{n}\beta_i x_i + \sum_{i=1}^{n}\sum_{i<j}^{n}\beta_{ij}x_i x_j + \sum_{i=1}^{n}\sum_{i<j}^{n}\delta_{ij}x_i x_j(x_i - x_j) + \sum_{k=1}^{n}\sum_{j>k}^{n}\sum_{i>j}^{n}\beta_{ijk}x_i x_j x_k \tag{6}$$

2.2. Optimality criterion

To fit some of the models it is necessary to select a group of n evaluation points. With n responses, we have n equations to fit the model. The number of parameters k must be lower than or equal to the number of experimental points. The model of Eq. (4) requires a system of n equations that is build up by Eq. (7).

$$\begin{aligned} y_1 &= \beta_1 x_{11} + \beta_2 x_{12} + \cdots + \beta_k x_{1k} \\ y_2 &= \beta_1 x_{21} + \beta_2 x_{22} + \cdots + \beta_k x_{2k} \\ &\vdots \\ y_n &= \beta_1 x_{n1} + \beta_2 x_{n2} + \cdots + \beta_k x_{nk} \end{aligned} \tag{7}$$

A specific DOE with n experimental points has k-parameters fitting the model, i.e. Eq. (1), which could be expressed as indicated by Eq. (8). The β coefficient vector that minimizes ε is the main fitting target. However in Optimal designs ε is reduced *a priori* by choosing the best selection of experimental points.

$$y = X\beta + \varepsilon \tag{8}$$

where

$$y = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix}, \qquad X = \begin{bmatrix} x_{11} & x_{12} & \cdots & x_{1k} \\ x_{21} & x_{22} & \cdots & x_{2k} \\ \vdots & \vdots & \ddots & \vdots \\ x_{n1} & x_{n2} & \cdots & x_{nk} \end{bmatrix}$$

$$\beta = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \beta_k \end{bmatrix} \quad \text{and} \quad \varepsilon = \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$$

In order to select the best n set of candidates from all possible ones, it is necessary to define an optimality criterion, this property could be approximated by maximizing i.e. $\det|X'X|$ [42]. The maximization of this determinant of the information matrix is known as the D-optimality criterion. Among a series of different groups with the highest $\det|X'X|$ the best D-optimal design for the fitting model may occur. There exist a variety of optimality criteria, and their use depends on the purpose of the DOE. For instance, if a high confidence on the variable effect estimation is required, a D-optimality must be chosen, but if it is desirable to get a high level of prediction, thus an I-optimality is recommended. These two criteria are based on the information matrix, X′X. The D-optimality criterion looks forward to maximize the information matrix in order to minimize the generalized variance of parameters estimation. Thus, in this work, the D-optimality was chosen to prove the ODOE.

2.3. Construction of the optimal design

To build up an optimal design one must determine a grid with all the possible experimental points. The variables ranges and a previous defined variable step size will help to determine it. For instance, a two-component catalyst is optimized by varying each component with a 0.02 step size, among 0.10–0.50 mol, thus 400 different concentrations are possible in catalyst. These 400 compositions constitute all the possibilities to explore. Finally, the experimenter accord the total number of experiments (n), and the k-parameters model to fit data ($k \leq n$), the search for the optimal design can start. The straightest way to find the optimal design for n-experiments, would be measure the optimality criterion for all combinations of n-experiments in the grid, i.e. $\det|X'X|$ for D-optimality. Since the X matrix is calculated from the fitting model selected, the optimal design is only the best for that model. Therefore, optimal designs are model dependants, .ing model is determinant. An important advantage is gotten when previous knowledge is incorporated to the model, i.e. a factor with a quadratic effect on response is known. For $n = 10$, in the example above described, 2.6×10^{19} optimality criterion evaluations would be required. Numerous search algorithms of the optimal design are based on valuing the contribution of each candidate point to the optimality criterion. A detailed review on these algorithms is presented by Cook [43]. Aguiar details an example drove by the Fedorov's algorithm [42].

When the process is too complex or too big, to be analyzed in only one DOE, a sequential series of DOEs is recommended. The first DOE must be directed to the screening of factors with low effect over the outcome. Once important factors and interactions are defined, additional experiments could be recommended. Then the following reduced DOEs expand the initial design, allowing the getting of a better fitting of the model, or outlining a narrow promising experimental zone [41]. The resulting DOE is known as an augmented design, and it is built based on previous experiments. A series of ODOEs are feasible to be conducted, because of ODOEs' features. Design augmentation is a technique to deploy a sequential series of Optimal DOEs [44]. Atkinson presents successful implementation of these techniques screening on optimization strategies [45].

2.4. Strategy's validation

Two hypothetical models that relate the performance with composition of a multi-component catalyst have been used, to evaluate a sequential series of ODOEs. The first model was previously used to validate the evolutionary approach (EA) proposed by Wolf [12], Eq. (9). This kind of models has also been proposed by other researchers, to evaluate their own strategy proposals [28,30,46]. The Miradatos' group has developed an open-source graphical interface for planning a driven search by a variety of stochastic methods, and Wolf's hypothetical method is also included. [17,47] Besides, some modifications to GA strategy have been proposed somewhere else [48].

This first model emulates the relationship between a catalyst formulation and its performance in oxidative dehydrogenation of propane. The catalyst is conformed as a mixture up to eight oxides (V_2O_5, MoO_3, MnO_2, Fe_2O_3, GaO, MgO, B_2O_3, La_2O_3). This mixture must follow the Eq. (3). Consequently, a mixture design [49] needs to be implemented, as traditional DOEs are not suitable. Among a short variety, the most used methods to handle mixtures are simplex centroid, simplex lattice and optimal mixture experimental designs; the reader is referred to a deep analysis of these methods in Refs. [50–52], an example of use in the discovery of heterogeneous catalysts is presented by Brycker [53]. Mixture experiments are the most suitable ones to make a DOE for a catalysis combinatorial experiment, because the mixture properties are more a function of relative proportion of ingredients than their absolute quantities. Therefore, it is impossible to make an independent change on a factor, without a modification over the others, as done in a classical experiment.

The Eq. (9) represents the Wolf's model. Where S_i is selectivity to propylene, X_i, corresponds to propane conversion, Y_i is the yield,

Table 1
Results of trained neural network to emulate propane conversion.

NN num.	Nodes	Parameters	Penalty (weight decay)	R_E^{2a}	R_V^{2b}	$R_E^2 \times R_V^2$	R_{FB}^{2c}
35	6	61	0.0002	0.9998	0.9656	0.9655	0.9994

[a] Least squares adjustment for training.
[b] Cross-validation.
[c] Full data set.

and i represents the type of preparation method used.

$$Y_1 = \begin{cases} S_1 \cdot X_1 & \text{if incipient wetness} \\ S_2 \cdot X_2 & \text{if coprecipitation} \\ 0 & \text{if } x_B \text{ or } x_{Ls} > 0 \end{cases} \quad (9)$$

with

$$S_1 = 66x_V x_{Mg}(1 - x_V - x_{Mg}) + 2x_{Mo} - 0.1x_{Mn} - 0.1x_{Fe} \quad (10)$$

$$X_1 = 66x_V x_{Mg}(1 - x_V - x_{Mg}) - 0.1x_{Mo} + 1.5x_{Mn} + 1.5x_{Fe} \quad (11)$$

$$S_2 = 60x_V x_{Mg}(1 - 1.3x_V - x_{Mg}) \quad (12)$$

$$X_1 = 60x_V x_{Mg}(1 - 1.3x_V - x_{Mg}) \quad (13)$$

2.5. Neural networks(NN) training

An extra validation method was configured by using a NN-meta-model, where the NN was trained with the data of a catalyst library published previously by Rodemerck et al. [14]. In that case a study was made with the purpose of finding a low-temperature catalyst formulation for the total combustion of propane traces in air (LTPO). The catalysts composition comprised some libraries that were set up as combinations of elements like Pt, Pd, Rh, Ru, Au, Cu, Ag and Mn, with supports like α-Fe_2O_3 or titania (TiO_2). The use of α-Fe_2O_3 was discarded after running the first two libraries, while Titania supported catalysts were further considered, thus, based upon an initial run with these data using our methods, the results obtained fitted well for this last library and that is why we decided to take this library instead of the whole set, i.e. see results for 150 °C in the multi-tube reactor in Table 3 [14]. A total of 45 catalyst formulations were used for NN training. Due to the complexity of multi-component catalyst synthesis, catalysts with 2–5 components were formulated but those having 4 components were more frequently used.

Also, a back-propagation method was used for the NN training while a Levenberg-Marquardt's algorithm optimized node weights. In order to avoid over-fitting topologies having only one-hidden layer and 5–15 nodes were considered. Thus, NN were optimized 16 times with different starting random points and each starting point was tested with five different overfit penalties, i.e., $(0.002)^i$, i = 1,2,..,5. 15% data were used for crossover testing, and a maximum of 100 iterations for convergence was considered. After 150 tries, a NN with (8-6-1) architecture was chosen as the best one to emulate propane conversion at 150 °C. The characteristics of this NN are shown in Table 1. For more information on NN applied to combinatorial catalysis the reader is referred to [54,55].

2.6. Research methodology

Fig. 1 shows the methodology of the present study, where two evaluations of ODOE were developed. The first one used Wolf's model to evaluate the prediction capability of an ODOE, while the second test emulated the fitness function by means of a trained neural network. Fig. 1 depicts the general procedure that was more appropriate for the second test because of its completeness. According to Fig. 1, the procedure was implemented from left to right and from top to bottom. The first step consisted of selecting an appropriate catalyst library from previous literature data and to pick up the results of reaction (block 1 and 2). Then, the NN was optimized to find an optimal formulation. On the other hand, the ODOE was configured to get a set of experiments that were evaluated using the NN-meta-model or the Wolf's model; afterwards the ODOE model was adjusted and optimized. The best formulation predicted by the ODOE model was compared to optimal formulation from NN model, i.e., blocks 4 and 9.

3. Results and discussion

3.1. Wolf's model

The blocks 1 and 2 belonging to the Wolf's group hypothetical model were saved for using them in the research methodology. The model optimization was performed and the best formulation was: 0.954 mol% V (0.318), 0.964 mol% Mg (0.3212), and 1.082 mol% Mo (0.3608), i.e., the numbers in parenthesis correspond to the normalized compositions. Fig. 2 depicts the estimated performance close to the zone of the best formulation, where the behavior in the experimental parameter space seems to be a similar multi-dimensional volcano zone, with the optimum corresponding to the top point.

In order to gain more information from the analysis of experimental results, an empirical model is usually considered, where the main task consist of optimizing the coefficients by training the NN system. However, if the data source is provided by a GA then the first library will be directed at least by the experimental points chosen at random. Additionally, if only a few generations are allowed to fulfill the search [12–15], then the uncertainty of the search of a global optimum increases. The improvement of the ODOE's experimental set will benefit of previous knowledge of the system. However, the fitting model must be chosen according to the main search objective. Thus, at the screening stage level the goal is to identify a reduced number of important factors while the precise parameter estimation is critical. On the opposite side, the optimal formulation requires a precise estimation of the predicted response.

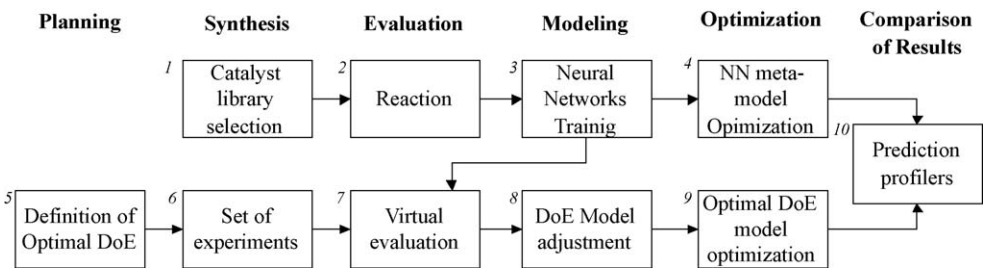

Fig. 1. Methodology's workflow.

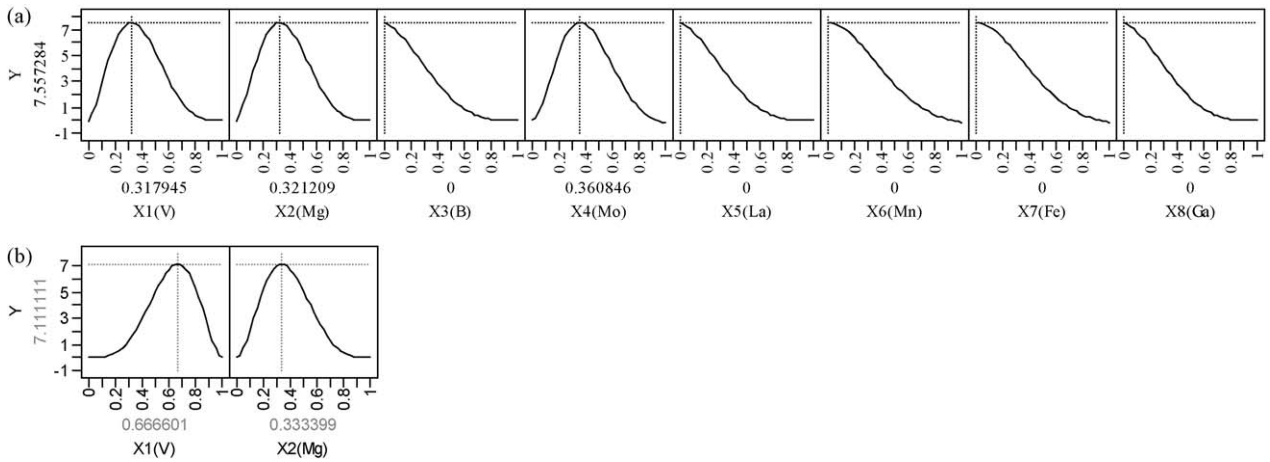

Fig. 2. Trace profilers for optimal formulation reached by Wolf's method: (a) incipient wetness, and (b) co-precipitation synthesis method. The crosshair is at optimal formulation. *Y*: propylene yield in mole percent; *Xi:* component concentrations in mole fraction.

3.2. D-optimal designs

The optimal designs configuration is based upon the reduction of some type of error from the information matrix, as described above. In turn, the information matrix depends on a model chosen to predict the phenomena. Also, the canonic models that are suitable for a mixture design are polynomial and, as expected, they are limited to represent all the types of experiments. Although this model dependence may rise some criticism [50,56], the exact model is unknown and a wide variety of nonlinear regression models have been studied to obtain the optimal functions [57].

3.3. Optimal designs for oxidative dehydrogenation of propane

Wolf's model represents a combination of both continuous and discrete variables. As oxides contributions are considered continuous variables while the preparation method itself is a discrete variable with two levels, i.e., incipient wetness and co-precipitation in Eq. (9), it was necessary to apply the ODOE to both levels of discrete variables. Thus, an ODOE based on the full Sheffe cubic model was build up using the coordinate exchange algorithm [58] and an experimental design of 120-experiments were proposed and applied to both models, with the purpose of comparing these results for selecting the best preparation method. Thus, Fig. 2 shows the hypothetical trace profiles of the Wolf's method solved (i.e., Eq. (9)) by means of the Levenberg-Marquard's method; these traces depict the multi-dimensional experimental space at the optimal formulation zone. A trace profile shows the predicted response in function of one specific variable while the other variable remains constant at the current values. Once applied the ODOE to both preparation methods, the fitted models were optimized and the trace profiles for the best formulations are presented in Fig. 3, where one observes that the more efficient ODOE is obtained for the best fit, even if the optimal formulations are not the same, but in both cases the space representation obtained by the ODOE optimization looks very similar to the reference model. Therefore, based on these results, the incipient wetness resulted the best method to prepare the catalyst and both models showed that the formulations obtained by the ODOE are too close to Wolf's model, thus further research was not followed. Furthermore, 240-experiments were required to optimize the catalyst formulation for oxidative dehydrogenation of propane, which means a 60% reduction on the number of experiments required by conventional GA methods.

A deep analysis of the ODOE for the incipient wetness method shows that the main difference with respect to Wolf's model (Fig. 2a) is the behavior shown by the Molybdenum concentration, which indicates that the optimum is shifted to the left hand side, i.e., lower concentrations of Mo. Also the upper part of the graphs corresponding to Mn and Fe is broader, which contributes

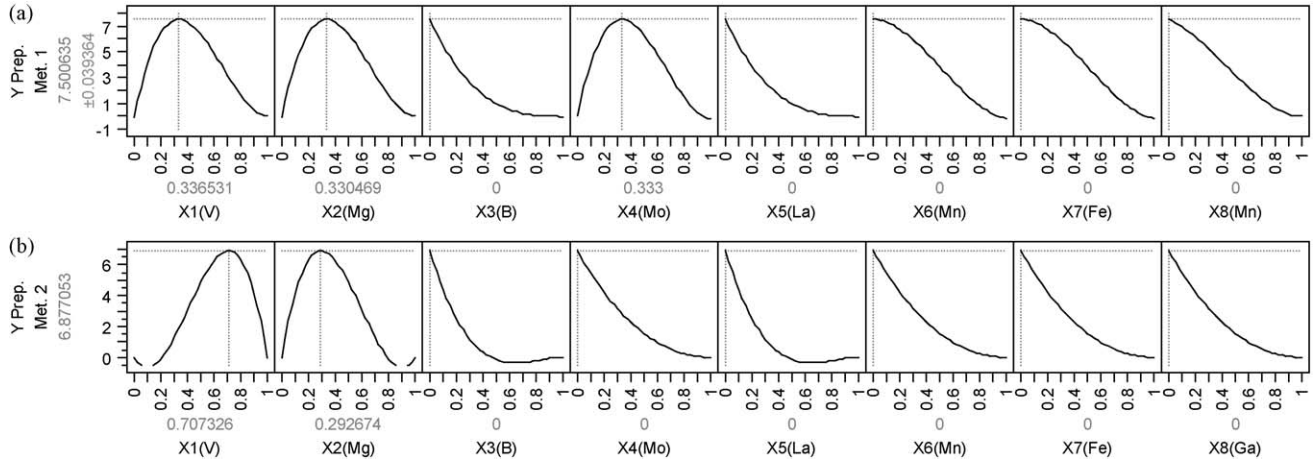

Fig. 3. Trace profilers for optimal formulations reached by 120-experiments ODOEs based on a three-interaction model, for Wolf's synthesis methods: (a) incipient wetness, and (b) co-precipitation. Crosshair is at optimal formulation. *Y*, propylene yield in mole percent, and *Xi*, component concentrations in mole fraction.

Table 2
Optimal formulations obtained for oxidative propane dehydrogenation.

Method	Num. of exp.	Component/composition								Wolf's model yield	Optimization method yield
		V	Mg	B	Mo	La	Mn	Fe	Ga		
Wolf[a]	n/a	0.318	0.321		0.361					7.56	
GA[b]	~600	0.320	0.320		0.260		0.05	0.05		7.53	7.53
ODOE[c]	240	0.337	0.330		0.333					7.50	7.50

[a] Mathematical optimization of the Wolf's hypothetical model, insipient wetness method.
[b] Evolutionary strategy proposed by Wolf [12].
[c] ODOE based on a full Sheffe cubic model for both preparation methods. All compositions are in mol fraction, and yield to propylene in mole %t.

significantly to reach the optimal formulation, for instance this formulation looks too similar to the one obtained by Wolf [12]. The Formulation results for the incipient wetness method are contrasted in Table 2.

Also, ODOEs may help to discard parameters with little or no influence at all on the response variable, which can extended the optimization furthermore. In order to prove this statement, an ODOE based on a two-interaction model using Eq. (5) was sequentially optimized. The model started with a design of 64-experiments and results of this first design are presented in Fig. 4a, where a visual analysis allows to discard B and La from the formulation. These two composition traces follow a convex behavior that reflects little or null effect in the optimal formulation, more significant effects are obtained when it approaches to cero. On the contrary, Mn, Fe and Mn traces follow a semi-volcano behavior with a maximum at cero, thus a low contribution of these elements to formulation is rather possible. The remaining elements dictate an extension to 8-experiments to achieve a second optimization of the proposed model (Fig. 4b), which allows to discard Fe from the optimized formulation. A last extension to eight additional experiments let to arrive to the closest optimal formulation for a two-interaction model (Fig. 4c). Since the results of the second and third design are not so different among themselves, a better result is not possible. With this example the upgrading through ODOE is proved, as well as the importance of the model selection to build up the design. In this case the selection of a two-interaction model has not been enough to accurately represent the catalytic system.

3.4. Optimal designs for total combustion of low-concentration propane in air

Based upon the optimization of trained NN, the best formulation for propane conversion was obtained and Fig. 5a shows the closest chemical space zone to that optimal point. This graph helps to notice how the optimal zone looks like. For instance, the behavior of Pd and Ru is not as smooth as the other components. On the other hand, Au has a flat shape at the top for concentrations lower than 0.2 mol fraction. These characteristics could drive the search to local optima, which are closer to the global one. However, the whole behavior seems to be smooth enough to be predicted by an ODOE model.

A Sheffe cubic model was utilized to study the catalytic propane conversion system. In order to include extra interactions with little or null effect on the catalyst performance; the model was reduced by omitting $x_i\,x_j\,x_k$ type interactions. Thus, a 64-experiment ODOE was proposed, which was evaluated later on using the trained NN.

The analysis of variance for the fitted DOE model is shown in Table 3, while Fig. 6 shows the predicted and actual values, where

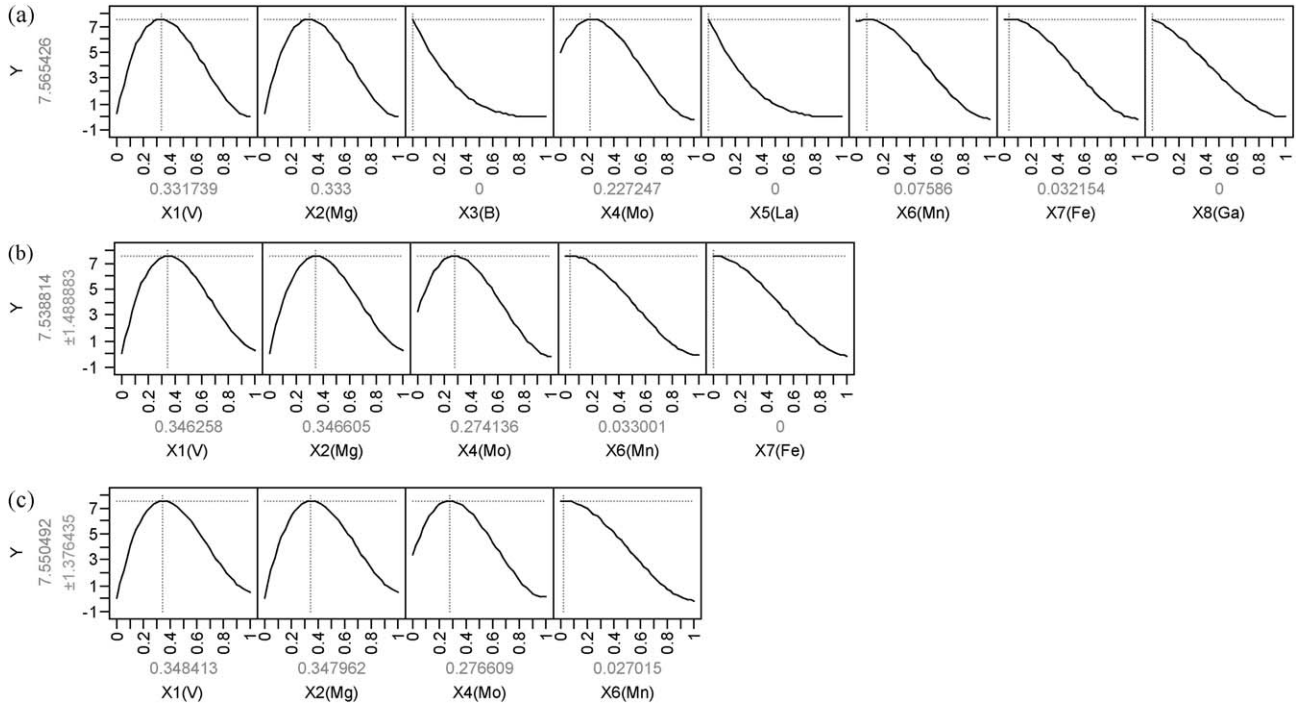

Fig. 4. Trace profiles for optimal formulations reached by sequential ODOEs based on two-interaction model, (a) original 64-experiments ODOE, (b) 72-experiments augmented extended ODOE, (c) 80-experiments augmented extended ODOE. Validation model: Wolf's incipient wetness synthesis method. Crosshair is at optimal formulation. *Y*, propylene yield in mole percent, and *Xi*, component concentrations in mole fraction.

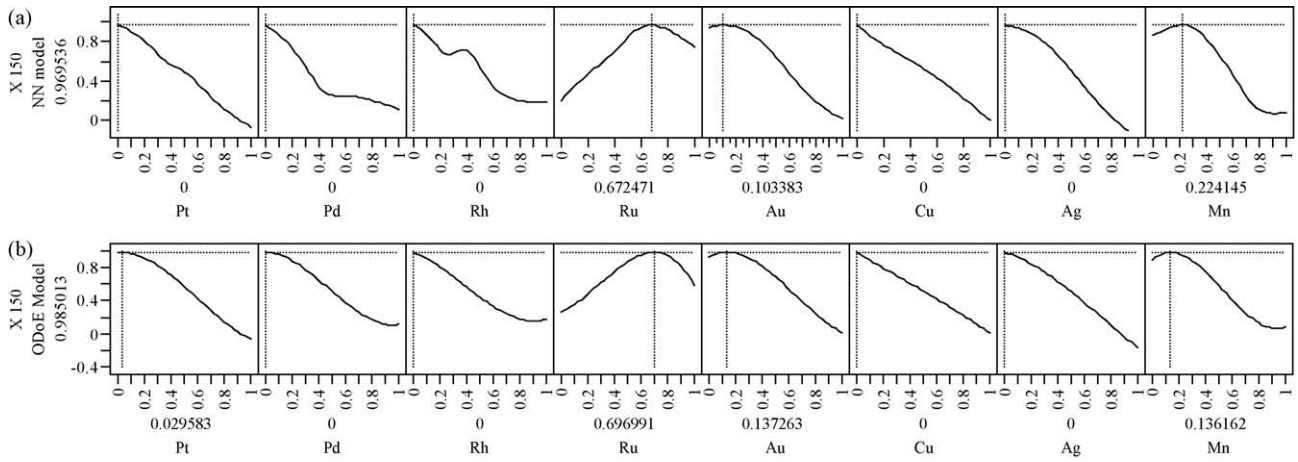

Fig. 5. Trace profilers for propane conversion for: (a) NN used as reference, and (b) ODOE model. The crosshair is located at optimal formulation. *X 150*, is propane conversion in mole percent at 150 °C. [14] Horizontal axis shows normalized component concentrations for a 3% metal content.

one observes a very good adjustment (1.00) and a very low predictive error. The estimation of the top ten influential parameters is also listed in Table 4. According to these data Rh has a very high influence in the catalyst performance and it also has a strong interaction with Au, Ag, Pd and Mn. However, it is interesting to note that Ru has also a high effect on the performance, but it does not present a significant interaction with Rh, though both elements show a great effect in combination with Ru and Au.

For the ODOE model Fig. 5b depicts the behavior of the catalyst component in the chemical zone that is the closest to the optimum. The predictors profile is alike to the one corresponding to the NN network, though Pd and Rh are not represented properly. The corresponding zones of these components were not completely emulated, which produces a smoothed curve instead of a rough one. Even if Rh has the greatest effect on the formulation, it was absent from the optimal formulation, possibly due to that lack of fitting.

Table 3
Analysis of variance for ODOE's model.

Source	DF	Sum of squares	Mean square	F ratio
Model	59	5.8602	0.0993	544.8
Error	4	0.0007	0.0002	**Prob>F**
C. total	63	5.8609		<.0001

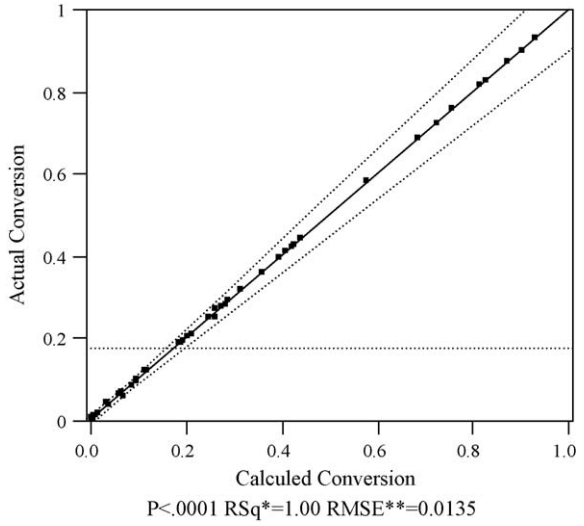

Fig. 6. Actual Conversion by means of the Predicted Plot for ODOE model. *RSq = rsquare **RMSE: root mean square error.

Table 4
Ten top influential parameters over the catalytic performance.

Term[a]	Estimate[b]	Std Error[c]	t ratio[d]	Prob>|t|[e]
Rh*Au*(Rh-Au)	−4.377	0.1221	−35.84	<.0001
Rh*Au	2.077	0.0637	32.59	<.0001
Rh*Ag	1.549	0.0663	23.35	<.0001
Pd*Rh	−1.344	0.0625	−21.49	<.0001
Cu*Mn	−1.313	0.0635	−20.66	<.0001
Ru	0.585	0.0296	19.72	<.0001
Ru*Mn*(Ru-Mn)	2.713	0.1396	19.42	<.0001
Pt*Ru	1.711	0.0890	19.22	<.0001
Ru*Au	1.774	0.0943	18.80	<.0001
Pt*Au*(Pt-Au)	−2.440	0.1323	−18.43	<.0001

[a] Mole fraction of component in catalytic formulation.
[b] Model's coefficient estimation.
[c] Standard error.
[d] *t* statistic ratio.
[e] Term's probability of being wrong estimated.

Table 5
Summary of optimal formulations obtained for total conversion of low concentration of propane in air.

Model	Num. of exp.	Component/composition								NN conv.	ODOE model conv.
		Pt	Pd	Rh	Ru	Au	Cu	Ag	Mn		
NN	n/a				0.673	0.103			0.224	0.969	0.962
ODOE	64	0.030			0.697	0.137			0.136	0.943	0.985

All the compositions and propane conversion are expressed in mole fraction.

Table 5 contrasts the optimal formulations obtained by the trained NN and ODOE model. Two main differences are observed, first the ODOE model proposes the necessary inclusion of an extra component, which is Pt, and a reduced contribution by Mn. This last deviation affects the propane conversion in the NN modeling, which is noticeable because the closest experimental parameter zone to optimum is alike to the reference one, thus it is better to search for a better estimation in a sequential second ODOE run.

4. Conclusions

In this work the ability of the ODOE method to optimize a formulation catalyst with a reduced number of experiments was explored as well as its capability of improvement through extra experiments. The results highlight the importance of the correct

model selection to build the design and all this demonstrates that ODOEs are practical alternatives for the catalysts library optimization.

A distinctive advantage of ODOE is its capability to include previous knowledge into the proposed model, i.e. a factor behavior is quadratic with respect to the response variable, thus a better fitting and system representation could be obtained by considering *a priory* this relationship into the model. The advantages of ODOEs are not limited to linear models only, since a wide variety of nonlinear regression models are available as optimal functions [57]. However, ODOEs' model dependency is also an inherent disadvantage because a wrong model selection could drive the search to erroneous conclusions with respect to the optimal formulation. Thus, ODOEs constitute alternative methods for facing the complex multi-dimensional problem such as the catalyst formulation optimization. The empirical models developed in ODOEs should provide the fundamental bases for obtaining mechanistic models of a specific catalytic system.

Contrary to GAs, ODOEs optimize the CLOM by the correct selection of experimental points. This feature reduces the number of experiments to be performed as proven in the present work. Also, ODOE has demonstrated its capability to handle both mixture experiments and type variable mixtures. Categorical variables could be included into the design or considered as independent experimental blocks. For the latter case, the post-treatment operations could be easy implemented because the experimental design is the same for all the blocks and one only set of untreated catalysts would be necessary.

Eventually, a confident simulation model for evaluation the newer optimization methodologies as those herein discussed will be necessary.

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