Descriptors for solid catalysts: 21st century discovery tools
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1 Heterogeneous catalyst discovery using 21st century tools*

1.1 Introduction

Research in the discovery of novel heterogeneous catalysts faces an enormous challenge in years to come. With the now commonly acknowledged abundance of fossil resources like shale gas, refineries around the world will shift their feedstock from oil to gas. This requires the need for novel catalytic pathways to for example C2-C4 olefins\textsuperscript{1-4} and aromatics.\textsuperscript{5-7} Where many of these molecules are now extracted from oil or its subsequent cracking product in the refining process, novel processes are needed considering light alkanes like methane, ethane and propane as the feedstock.\textsuperscript{8,9} Concurrently, the field of biomass conversion is also maturing. Several processes producing building blocks based on biomass will come online in the next two decades. In this area, catalytic processes are required to convert these building blocks to products. These products include both drop-ins like ethylene from ethanol,\textsuperscript{10} butanediol from succinic acid \textsuperscript{11} and aromatics from alcohols \textsuperscript{12} as well as new-to-world products like furan dicarboxylic acid \textsuperscript{13,14} (FDCA) to be used a novel monomer for polyesters and farnesene \textsuperscript{15,16} to be used as a novel fuel and lubricant component. Regardless the nature of the final product – catalysis is typically required to perform the final steps of the process.

Since catalysis research is a multifaceted problem, involving variations in catalyst composition and experimental conditions, a systematic research methodology is required. Doing only experiments is not efficient. Instead, the use of modelling methods of various degrees of complexity is recommended to effectively discover new catalysts for new or existing processes.

Applying modelling methods will benefit all stages of catalyst development, provided that the appropriate level of complexity is applied at each stage. As a general rule, model complexity should increase as a project progresses. Initial stages need relatively simple methods from chemometrics (exploratory data analysis) and experimental design (empirical modelling). Later

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stages will benefit from more rigorous, kinetic models. Note that the “users” of models and data differ at the various stages. In early stages, the target audience is mostly composed of research chemists. At later stages, the focus shifts to providing chemical engineers with sufficient information to design pilot-scale processes. Involving the engineers from the start is the key to success. 17,18

This work focuses on empirical modelling methods, illustrating them with three case studies: First, we discuss statistical experimental design on the oxidative coupling of methane. This chemistry is receiving an increased amount of attention in both academia and industry 19-21 with the expected price developments for methane resulting from shale gas production. Then, we review the use of exploratory data analysis with principal component analysis (PCA) and descriptor-performance relationships using hydrogenation of 5-ethoxymethylfurfural (EMF). 22-24 Finally, we explain the development of generic descriptors for metals using a computationally-derived database of heats of adsorption of gases on metals. 25 The latter approach is then validated by evaluating its performance against the experimentally measured adsorption of gases on titania-supported metals.

Note that while a part of this work focuses on using large data sets generated by parallel reactor technology, our primary objective is not explaining high-throughput experimentation. Instead, we focus on data analysis and modelling methods that help to maximize learning from these large data sets. Specific information on the various uses, strengths and weaknesses of parallel reactors are available elsewhere. 18,26-28
1.2 Typical workflow for catalyst development

To understand better the use of empirical modelling methods, let us first examine the unit operations of the typical workflow for catalyst development (Figure 1). The guiding principle of this workflow is that it is an iterative process, not a linear one. After each set of experiments, the results are compared against the objectives. If these are met, you may proceed to next stage. Otherwise, if the data indicates that your initial objectives are unrealistic, these objectives must be adjusted.

![Flow diagram representing a typical workflow for the development of catalysts.](image)

**Figure 1** Flow diagram representing a typical workflow for the development of catalysts.

The empirical modelling methods (highlighted in green in Figure 1) are the focus of this work. We also discuss briefly some other elements of the workflow, namely catalyst synthesis and testing.
Typical precursor selection and catalyst synthesis considerations

The key to a successful scale-up of catalyst synthesis is in the simplicity of the methods used. Straightforward steps like impregnation and precipitation can be scaled up relatively quickly to produce kilograms of catalyst. Even for the simplest impregnation (Figure 2) a large number of steps and variables have to be considered. Since many excellent books have been published on this subject, we only highlight a few key points here.

First, we consider the starting materials. Commercially accessible materials are preferable. This holds for both the carrier, in the case of a supported catalyst, and for the metal precursors. We also keep in mind the conditions that the catalyst will be exposed to during its synthesis and testing. The support must maintain its structural integrity during calcination and reduction. Well known examples include the anatase-rutile transformation observed for titania and ceria structural collapse at high temperature. The precursor salt should be readily transformed to an oxide or metal during calcination and/or reduction. As a rule of thumb, metal nitrates are preferable over chlorides. Most nitrates require calcination temperatures between 250 and 400 °C, while chlorides typically require temperatures between 500 and 700 °C. If a metal is prone to sintering or agglomeration, its chloride precursor is more likely to give a lower active metal surface area. Likewise, organic anions such as acetate or oxalate introduce the risk of carbon deposits on the catalysts. Examples of catalysts that can be synthesized using straightforward methods in the laboratory are Pd/Al₂O₃ for hydrogenation, AuPd/SiO₂ for vinyl acetate synthesis from acetic acid and ethylene, and Cu-chromite for furfural hydrogenation.

The accuracy of small-scale preparations (milligrams to grams of catalyst) benefits from minimizing the number of steps (i.e. running a more dilute, single-step impregnation). In the case of bimetallic (or multimetallic) catalysts you must choose between single-step (co-impregnation) and sequential impregnation. We advise trying out both methods on a small number of catalysts before preparing large libraries.
Co-impregnation is simpler, but sequential impregnation is preferable when the difference in solubility for two precursor salts is large. One such example is the synthesis of the supported Pt-Sn catalyst used in the reduction of α,β-unsaturated aldehydes and the dehydrogenation of alkenes to olefins or aromatics. Here the solubility of platinum nitrate is high, while the solubility of tin acetate is low. Unless you need very low tin loadings, this impregnation requires two (or more) steps. 36, 37

**Figure 2** Typical steps in catalyst synthesis via impregnation. Note that some steps, in particular the dissolution and impregnation, may need to be carried out multiple times.

**Typical catalyst testing considerations**

When testing a catalyst library, defining a uniform test protocol is important. Here the key parameters are the activation procedure, the catalysts' stability, the reference conditions, and the analysis methods. In the following paragraphs we briefly address these topics. A more detailed discussion of common synthesis methods is given in the books edited by Ertl 29 and Regalbuto. 30

First, let us consider the catalyst activation procedure. Often, a simple reduction step followed by a short equilibration with the feedstock will suffice. One notable exception is hydrodesulfurization, which requires a sulfiding step using a sulfur donor (typically H₂S or Me₂S). Another is the Fischer-Tropsch synthesis, where the catalyst must be equilibrated under reaction conditions for up to two weeks before reaching steady-state performance. 38 While the optimal activation method may differ between individual catalysts, using a consistent testing method makes comparing the performance data easier. 39

The second factor we must consider is catalyst stability. If catalysts are known to have a limited lifetime, the number of experimental conditions that can be explored needs to be limited. In case lifetime is not a concern, longer run times can be used and thus more data points per catalysts can be obtained. In a flow reactor the experimental conditions that can easily be varied on stream
are a) temperature b) space velocity c) pressure and d) feed composition. If the experimental conditions are varied during testing, you must frequently return to a reference condition with known performance. As long as this performance does not change, you can assume the catalyst has not changed.¹⁸

In most cases, the compositional analysis of products is the bottleneck of catalyst testing. This is true even for simple gas-phase reactions. The common techniques are chromatography and spectroscopy. The key advantage of chromatography is that the components in the reactor effluent are separated and thus easily quantified. The disadvantage is the time-consuming analysis. Assuming the composition of reactor effluent can be determined in five minutes using GC, one still needs over five hours to analyse 64 reactors.⁴⁰ Conversely, spectroscopic analysis enjoys the advantage of speed, but suffers from the fact that all components are analyzed simultaneously. This means the concentrations of individual components must be extracted by means of multivariate calibration and/or deconvolution. ⁴¹,⁴²

1.3 Integrating modeling methods in catalyst research

For clarification, we will divide the modelling methods in catalysis in two groups: fundamental and empirical (Figure 3). The first group, which includes computational chemistry, kinetic models and reactor design, focuses on reaction mechanisms and engineering principles. Such methods are useful when mechanistic information and/or reactor constraints are available a priori. The second group includes data-driven models that make no assumptions on reaction mechanism or the reactor configuration. They can therefore be applied early in the research when little information is available.

In contrast to popular belief, modelling methods in catalysis are best used in an integrated manner. Synergy is achieved only by close collaboration between the modelling and experimental teams. The largest hurdle here is the “language barrier” between researchers from different disciplines. Strikingly, the empirical (data-driven) methods pose the most difficulties. This is because they are typically practiced by statisticians rather than chemists or chemical engineers. In this tutorial, we will highlight the useful information obtainable by combining empirical models with experiments.
Figure 3 Modeling methods used in catalysis research. The empirical methods are highlighted in green on the right hand side of the diagram. The more fundamental methods are located on the left hand side of the diagram.

Statistical experimental design

Using appropriate experimental design methods will increase the chances of success for a project in all its stages, from very early screening to the final optimization of catalyst composition and process conditions. The key here is selecting the proper variables. The more complex your system, the more experiments you’ll need for exploring the parameter space. But experimental design does much more than just minimize the number of experiments. It also ensures that you run the correct type of experiments.

A typical experimental design campaign has three main stages: (1) factor screening, (2) optimization and (3) robustness testing. During factor screening, a large number of variables is explored using a small number of experiments. The objective here is eliminating variables that have only a small on the performance. Only the variables that remain progress to stage (2), the optimization stage. This stage then provides a quantitative relationship between the variables and the responses. The robustness stage (3) is a sensitivity analysis, providing assessing the expected stability of the optimized system.
Figure 4 Raw performance data for the oxidative coupling of methane over a Mn-promoted Na$_2$WO$_4$/SiO$_2$ catalyst. The vertical axis denotes the combined yield of ethylene and ethane. The horizontal axis denotes the conversion of methane. Marker color denotes the reaction temperature and marker size denotes the reaction pressure. The plot is split in panels based on the space velocity used during the experiment.
A good experimental design also allows the data to be analyzed as a model instead of as a mere collection of data points. As an example, let us consider the behaviour of a Mn-promoted Na₃WO₄/SiO₂ catalyst in the oxidative coupling of methane. We tested this catalyst in 64-channel parallel fixed bed reactor at various experimental conditions. The temperature was varied over the range 755-875°C, the pressure over the range 0-2.5 barg, the GHSV over the range 6000-36000 h⁻¹ and the methane to oxygen stoichiometry over the range 4-8 molar equivalents. With so many variations, the raw data for even a single catalyst is overwhelmingly complex (Figure 4).

However, since the conditions were varied systematically, we can calculate a response surface model. Here, the parameters (temperature, pressure, GHSV and stoichiometry) are related to the responses (conversion, yields, selectivities). The resulting models can be used to identify the optimal conditions will give optimal performance. As an example, Figure 5 shows a set of response surfaces based on the data shown in Figure 4. We see that the highest methane conversions are found at the lowest space velocities combined with the highest temperature. Less obvious from the raw data, but very clear from the response surfaces: the temperature required to achieve maximum C₂ yield shifts from 875°C at 0 barg to 825°C at 2.5 barg. Another important observation is that the absolute maximum C₂ yield is 16% at 2.5 barg, whereas at 0 barg a maximum yield of 19% can be obtained. For clarity, we show here only two of the key responses, but the other two (CO₂ selectivity and ethylene/ethane ratio) can also be described by similar models.

Note that response surface models typically use continuous parameters and responses. When categorical parameters are used (for example “good” or “bad” performance or "support 1" and "support 2"), separate response surfaces have to be constructed for each setting. Alternatively, one can use classification models.
Figure 5 Response surfaces for the CH₄ conversion (bottom row) and C₂ yield (top row) at 0 barg (left column) and 2.5 barg (right column) as a function of temperature (vertical axis) and GHSV (horizontal axis). The value of the responses is mapped using the color scale on the right hand side of each panel. The CH₄ to O₂ ratio used to construct the plots equals 4. The white area in the plots at 0 barg indicate predicted conversion and selectivity < 0%.
Explorative data analysis

Data overload is a big problem with parallel experiments. The best solution is using a database for storage and combination of data. Database platforms (for example SQL, Oracle, MySQL or even Microsoft Access) have many benefits over simple spreadsheets. The most important of these is the ease of linking and combining information from various sources into a single table. Information on the materials used, catalyst synthesis, experimental conditions, raw analytical data and calibration data must all be combined into a single table that tells you what the performance of each of the catalysts tested is at each experimental condition.

Once the data set is constructed the initial visual exploration of the data can start. Here the total data set needs to be considered. Particular attention is needed for the identifying outliers. These must be studied, and where appropriate removed prior to any model-based data analysis. In this stage it is also important to check the stability of process parameters like temperature and pressure. Several commercial software packages are available to facilitate the visual interpretation of data (for example Spotfire, Miner3D and Tableau). However, keep in mind that interpreting plots mapping many dimensions can be difficult (Figure 4, for example, was generated using Miner3D and is a typical multi-dimensional representation of data).

**Figure 6** PCA reduces the dimensionality of the problem by projecting the original dataset onto a lower-dimension PC model, in which the new variables are orthogonal to each other. The concept is illustrated here by the transformation of the 3-variable raw data (left) to the 2-component scores (right).
Once the initial exploration of the data set is complete, model-based evaluation can start. One of the most common methods here is principal component analysis (PCA). PCA aims to reduce the number of dimensions of a data set whilst preserving as much as possible the variability. Using PCA, you can extract the key factors. These are the principal components, or PCs (sometimes also called the latent variables). Each PC is a linear combination of the original variables, but unlike the original variables, which may be correlated with each other, the PCs are orthogonal (i.e., uncorrelated, independent of one another, see Figure 6).

To demonstrate the usefulness of PCA, we show the data and PCA analysis thereof for the selective hydrogenation of 5-ethoxymethyl furfural (EMF). As with all \( \alpha,\beta \)-unsaturated aldehydes, the primary reaction products are an unsaturated alcohol and a saturated aldehyde. Both primary products undergo various sequential hydrogenation and hydrogenolysis reactions, resulting in a rather complex reaction network (see Figure 7) with eight products occurring in significant amounts (>5% molar yield). In this case only two principal components are needed to explain 70% of the variation in the data. That means that interpreting the data for a large part can be done by looking at a single two-dimensional plot of the PCs, which is an easier task than identifying trends in the original eight conversion-selectivity plots. A brief explanation of PCA is given below, a more detailed treatment in the context of this data set is given in Chapter 3.

PCA gives us in two pieces of information: First, the loadings (P) tell us how the individual yields contribute to the structure of the data set. From the loadings plot we can learn a number of things (Figure 7). First, we see that the loadings for all yields are positive in the first principal component (the horizontal axis in Figure 7) – this indicates that all yields go up in this direction, in other words PC1 primarily gives information about activity. When considering PC2 the loadings for the yields of 3 and 8 are almost at the same coordinate. This indicates that, no matter what changes are made to catalyst or conditions, the yields of these two components will always increase or decrease together. This is important, because if the objective is maximizing the yield of one of these products alone, the PCA model tells us this will likely be impossible.
Second, the scores on the principal components (T) tell us how each observation relates to the total data set. Since here we base our PCA model on the yields, if two data points are close together in scores space they will have a similar product distribution. In contrast, if they are far apart they will have a rather different product composition. This is easily demonstrated using the scores plot (Figure 8). Here we see two distinct clusters. The cluster in the upper right quadrant corresponds to a set of Pd/Al₂O₃ catalysts with various promoters tested at temperatures of 100 and 120°C. At these temperatures this group catalysts favours ring hydrogenation. The cluster in the bottom right quadrant is composed of a set of Rh/Al₂O₃ and Pt/Al₂O₃ catalysts tested at 120°C. The common denominator here is the preference of these catalysts to only produce carbonyl reduction products, leaving the furan ring intact. Both clusters are on the right hand side of the plot, indicating (near) complete conversion.

**Figure 7** Loadings for the individual yields of products 2-8 occurring in the selective hydrogenation of EMF (left) and the reaction network for the reaction (right)
Figure 8 Scores plot for the PCA model with the markers colored as a function of the main metal used for each catalyst.

The explorative data analysis using PCA is elaborated further upon in Chapter 3. This type of analysis is an important data pre-processing step when more elaborated data analysis methods like response surface modelling (preceding section in this Chapter) and descriptor performance methods (Chapters 4 and 5) are to be used. Not only outliers can be identified, but also an assessment can be made whether the data can be captured in a single model. If this is not the case, one can identify in which region of the data additional data is needed, or what is the best method for splitting the data into subsets.
Descriptor-performance relationships for heterogeneous catalysis

The development of descriptor performance relationships for heterogeneous catalysts is hampered by the fact that the active site of a heterogeneous complex is often poorly defined. In contrast, in homogeneous catalysis the entire catalyst is a well defined, molecular complex that can readily be described by common computational chemistry software. This is reflected in the number of publications describing successful applications. For homogeneous catalysis, the last 20 years yielded many published examples and reviews.\textsuperscript{45-48} For heterogeneous catalysis examples are scarce.\textsuperscript{49, 50} A large number of publications based on the use of density functional theory (DFT) are available.\textsuperscript{51-53} Although valuable to gain fundamental insights, using these methods in virtual screening for new catalysts is limited due to the demanding nature of these computations.\textsuperscript{54} In fact, in the time required to model even a small number of catalysts using DFT, many catalysts can be synthesized and tested in real life. Despite all this using simple, readily accessible descriptors for the metals on the catalyst surface can provide a meaningful means of creating descriptor-performance relationships.

One of the most important differences between heterogeneous and homogeneous catalysis in descriptor modelling is the maturity of the available tools. In homogeneous catalysis, the last two decades of research have resulted in many theoretical descriptors. These range in complexity from simple atom and group counts to topological maps derived from graph theory to geometrical descriptors of varying complexity. Open source and commercial software packages are readily available. In heterogeneous catalysis this is different. Here available descriptors are often difficult to obtain and are typically derived from DFT studies or extensive characterization of the catalysts. These methods, albeit of tremendous value to provide fundamental insights, are time consuming and require specialist knowledge. Catalyst characterization as a means to derive descriptors related to performance poses another issue: one first needs to synthesize a catalyst, making “virtual screening” a challenging task.\textsuperscript{54}

Underlying these challenges in heterogeneous catalysis is the nature of the catalyst. In homogeneous catalysis, catalysts are typically well-defined molecular complexes. In heterogeneous catalysis typically a much more complex situation is encountered, where support and metals each play multiple roles.
An example - the selective hydrogenation of 5-ethoxymethylfurfural (EMF)

One practical approach, which we presented for assigning descriptors for modelling heterogeneous catalysts, is using simple bulk properties of the metals. We showed recently that even a complex reaction like the hydrogenation of EMF (Scheme 1) can be described by correlation of bulk properties of the metals used with the yields of the main components. To simplify the problem, we kept the support material and catalyst synthesis method used constant. This allows us to focus our efforts in terms of descriptors on the metals used alone. The descriptors we used were derived from Slater-type orbitals for the metals. Instead of using the entire orbital function, we describe the curve by a number of peak parameters often encountered in chromatography and spectroscopy. These simple parameters, the magnitude and location of the peak apex, the width at half height and the skewness, are surprisingly well capable of correlating the metal used with the yields of the main products of the reaction. To establish the validity of the method we first explored a small data set for monometallic catalysts (Figure 9). After establishing that this model performs well, we extended the data set to bimetallic catalysts and again, good model performance was obtained.

One important characteristic of empirical modelling methods needs to be emphasized here. Since there is no underlying theoretical model describing the reaction, an empirical model will happily predict negative yields or conversions exceeding 100%. This means that such a model should always be validated chemically and statistically. Luckily, most statistical modelling methods provide this information as an integrated part of the method. When using these methods to design a next set of catalysts for further testing a special situation occurs.
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Scheme 1 Extended reaction network with the main products observed in the selective hydrogenation of EMF 1 to the unsaturated alcohol 2.
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For any empirical model a simple rule of thumb is that predictions can be made only over the range of data that was used to create the model. In other words, if a model is regressed using data over a yield range of 0 to 70%, that model will not be able to reliably predict yields greater than 70%. Thus, if the objective for a next set of catalysts is increasing the yield beyond 70%, you need to extrapolate. In practice, each next set of catalysts will be based on predicted performance just outside the current range of data. By refitting the model after each set of experiments the valid yield range for the model is extended in an iterative manner.

Figure 9 Matrix plot comparing observed yields (left) to the yields predicted by the OPLS model (right). The products are grouped in columns, the catalysts and temperatures are grouped in rows. The yields are coded from light (low yield) to dark (high yield). Both predicted and observed yields are plotted on the same scale. On the right hand side a parity plot representing the same information is given to facilitate interpretation.

The descriptors based on Slater-type orbitals developed here demonstrate that it is possible to find functional descriptors for heterogeneous catalysts using light weight computational methods only. This method is discussed in detail in Chapter 5.
Developing new descriptors

In contrast to the field of homogenous catalysis, the scientific literature documenting descriptors for heterogeneous catalysts is sparse. Several groups published successful examples of the application of DFT simulations to describe reaction networks. Application of the d-band center as a descriptor is also referred to in many occasions. When turning our attention to simple, empirical descriptors the number of references is even lower. On the basis of this less than abundant literature it is safe to assume that there is a need for documented cases of descriptor development. For these cases it would be important that not only their application is documented, but also sufficient information is provided to allow a researcher to use and extent the method in their own work. As an example, we present here the development of descriptors related to adsorption of gases on metal surfaces. Here we developed an empirical model to describe a large database of DFT computations, coupling the heats of chemisorption of 10 different gases to simple, tabulated properties of these gases and the 13 different metals. Using this correlation (Figure 10) between descriptors and computationally derived chemisorption data, we then extended the method to experimental data obtained using real catalysts, and proven sufficiently robust for application as a more general set of descriptors.

![Figure 10](image-url)

**Figure 10** Comparison of the heats of chemisorption obtained using DFT (left) and a simple empirical model based on descriptors (right). The cells with dots indicate the metal-adsorptive combinations that have been used to construct the empirical model.
This empirical correlation that links easily obtained properties to a phenomenon that is crucial to heterogeneous catalysis, is valuable. Without extensive computations, one can quickly test a few ideas and get a feel for their viability, thus saving the experiments for those ideas that have most merit. As with any empirical model, one has to consider its range of applicability. Luckily, the modelling methods used to establish these models provide an assessment of how valid a prediction is. Moreover, if a prediction is invalid, the same statistics can be used to design a set of experiments (or computations) that allow extension of the model in the desired direction.

Note that the example shown is, indeed, just an example. Many different types of descriptors are typically needed to describe a problem. This is true especially when the catalyst attributes associated with good performance are not well known upfront and have to be established experimentally. When developing descriptors two guiding principles should be considered: 1) a set of descriptors should be accessible for most (preferably all) metals used in catalysis and 2) it should be sufficiently powerful in explaining catalyst performance on its own. The first guideline is easily explained. Imagine using three blocks of descriptors, each having a limited set of metals to which they can be applied. The search space that can be addressed using these descriptors is limited to those metals that can be captured by all three descriptor blocks. The second guideline is more complex. Since typically many different attributes need to be taken into account to explain catalyst performance, the correlation with activity or selectivity of a single attribute is often weak. In those cases, one needs to focus on significance of a correlation (or covariance) rather than its magnitude. Luckily, in the field of homogeneous catalysis these procedures have been tried and tested.

This example is elaborated upon further in Chapter 4. Here we also show that, although impractical for large scale virtual screening, high-end computations are extremely useful to serve as the basis for descriptor development by extracting empirical relationships. The same is true for detailed catalyst characterization methods. Although impractical as a predictive method – a catalyst first needs to be synthesized and characterized – using statistically designed sets of materials for characterization and subsequent development of empirical relationships works well.
1.4 References