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Catalyst design: knowledge extraction from high-throughput experimentation

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Abstract

We present a new framework for catalyst design that integrates computer-aided extraction of knowledge with high-throughput experimentation (HTE) and expert knowledge to realize the full benefit of HTE. We describe the current state of HTE and illustrate its speed and accuracy using an FTIR imaging system for oxidation of CO over metals. However, data is just information and not knowledge. In order to more effectively extract knowledge from HTE data, we propose a framework that, through advanced models and novel software architectures, strives to approximate the thought processes of the human expert. In the *forward* model the underlying chemistry is described as *rules* and the data or predictions as *features*. We discuss how our modeling framework—via a knowledge extraction (KE) engine—transparently maps *rules*-to-equations-to-parameters-to-*features* as part of the forward model. We show that our KE engine is capable of robust, automated model refinement, when modeled features do not match the experimental features. Further, when multiple models exist that can describe experimental data, new sets of HTE can be suggested. Thus, the KE engine improves (i) selection of chemistry *rules* and (ii) the completeness of the HTE data set as the model and data converge. We demonstrate the validity of the KE engine and model refinement capabilities using the production of aromatics from propane on H-ZSM-5. We also discuss how the framework applies to the *inverse* model, in order to meet the design challenge of predicting catalyst compositions for desired performance.

Keywords: Catalyst design; High throughput experimentation; Zeolite; Knowledge extraction

1. Introduction

We define materials design, which includes the design of catalytic materials, as a rational framework with associated tools for determining the optimum material and/or formulation to meet a given set of design objectives. Materials Design has significant differences from the more traditional design of electrical circuits/hardware, mechanical devices, chemical manufacturing, etc. Specifically, in traditional design, the component behavior (i.e., an individual transistor, mechanical linkage, etc.) is well known, while in materials design the determination of a model of the material behavior is often the most significant challenge. Also, the vast array of possible chemical structures/formulations leads to combinatorial complexity that dwarfs more traditional design problems. As shown in Fig. 1, materials design has two components: (i) a *forward* model that relates the chemical composition and/or high-level descriptors of the composition to the performance of the material in the application of interest and (ii) an *inverse* model that relates the performance to the desired chemical composition or formulation. Design is by definition the solution of the inverse model. Although solution of the inverse problem is often the primary technological

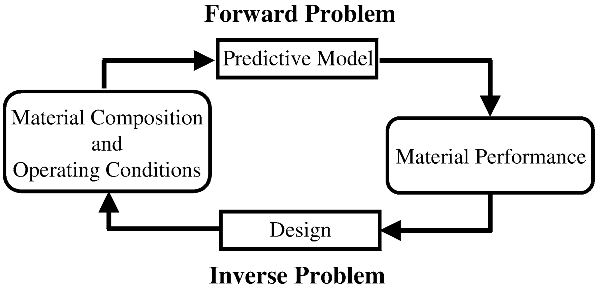

Fig. 1. Schematic of the forward and inverse problems in materials design.

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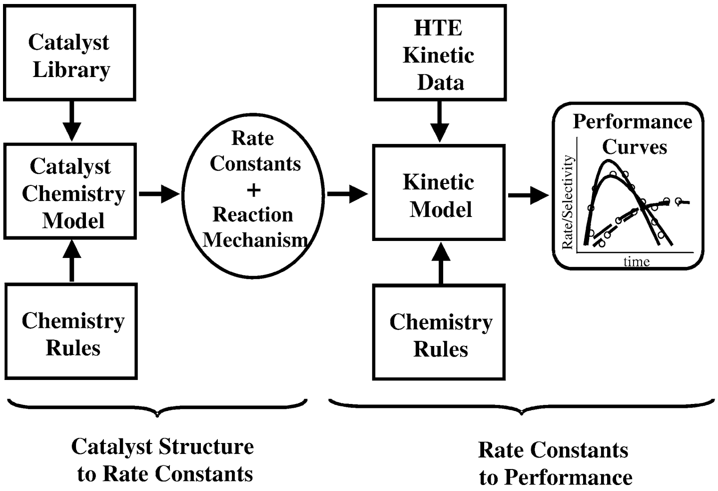

Fig. 2. Schematic of the overall forward model for catalyst design.

objective, rational vs Edisonian design methods require the availability of good, robust forward models, and the development of good forward models will require in-depth knowledge of the material system of interest. The objective of this paper is to examine the development of computer-based systems for the particular case of catalyst design—systems that can begin to take full advantage of the rate of data generation offered by high-throughput experiments (HTE).

Our group has developed materials design systems in several application areas, including polymers [1], gasoline additives [2], and formulated rubbers [3]. As an example, we summarize the problem of designing gasoline additives to minimize intake valve deposit (IVD) in an EPA-mandated test. The forward problem involved the development of a model to determine how changes in chemical structure of an additive mixture altered the degradation behavior in a complex engine environment. Using a hybrid model that included first principles models of the relevant chemistry with a neural network to circumvent the need for a detailed engine model, we were able to develop a one-parameter descriptor related to the thermal stability of the solubility character of the additive, which, in conjunction with limited engine data, could describe the IVD within experimental error. Using this forward model, we developed a genetic-algorithm-based search procedure for the inverse problem and found a variety of readily synthesized chemical structures to meet a target IVD—structures that had eluded the company's best formulation chemists [2].

Because of the success of the materials design approach for other complex chemical systems, we are now interested in adapting this approach to catalyst design. The forward model for catalyst design will involve two components, as shown in Fig. 2: a *catalyst chemistry model* that relates the chemical composition or high-level descriptors of composition (e.g., electron sharing indices) to the kinetic rate constants and a *kinetics model* that maps the reaction network to the catalyst performance. Because there is often uncertainty in the chemical/morphological state of the catalyst, the development of the catalyst chemistry model poses some unique challenges. First principles models using quantum chemistry alone may be insufficient, and while a large and diverse data set is essential, purely data-driven models will also probably be insufficient. Because of these difficulties, advanced modeling techniques will be required, where first principles models are used in concert with data-driven models. Relatively simple versions of these hybrid models were effective in addressing the gasoline additive design problem [2], but more sophisticated knowledge architectures will be needed for catalyst design. The kinetic model involves the determination of rate constants from experimental data assuming a particular reaction mechanism and thus connects with the catalyst chemistry model, where rate constants are determined from catalyst descriptors. It might appear attractive to just eliminate both the catalyst chemistry and kinetic models and attempt to directly correlate descriptors of the catalyst with the catalyst performance; however, in our experience all available knowledge is needed in order to reliably extrapolate to new regions of composition space, which is the essence of materials design.

We define the model as a clear, precise representation of knowledge, including first principles, data-driven, and expert knowledge; i.e., the model is a quantitative representation of knowledge about the catalytic system. If one wants the full benefits of HTE and the ability to do design, there is no alternative to model development. First, the composition space, even for a limited class of catalysts, can be so large that even HTE cannot fully search it. Second, if HTE is to lead to more than just correlations, knowledge must be extracted, and the knowledge extraction must be automated in order to keep pace with the flood of data that are becoming available via HTE. Finally, because of the complexity of the catalytic systems being modeled, the number of ideas that must be addressed simultaneously often exceeds the capacity of human experts. Consequently, a computer-aided knowledge extraction (KE) engine with both capabilities for model refinement and formulation of new, critical HTE experiments is a necessary component for effective catalyst design.

Finally, KE is not just a model, but rather a process—a process that starts with an incomplete model with potential errors and limited data, where each iteration of the process develops both a better model and more discriminating HTE data. It is the continued interplay between theory and experiment via both a computer-based system and human experts that results in the generation of new knowledge. If the KE engine, HTE data and the human expert are working in concert, the process should begin to converge with each cycle of the process.

The remainder of this paper is organized as follows: We will first present a brief review of the state of the art for HTE and then describe a new FTIR method for generating high-quality data. Subsequently, we will describe our work to date in developing a computer-based KE engine for catalyst development, after briefly reviewing the state of the art. Finally, we will provide a brief summary.

2. High-throughput experimentation

High-throughput screening of catalysts began almost 20 years ago, when Creer et al. [4] screened zeolite catalysts for cyclopropane conversion in a multichannel microreactor set-up. While parallel reactors have been run for many years, several new analytical approaches to high-throughput experimentation (HTE) have emerged in recent years. These aim to rapidly and efficiently screen known compositions of catalysts and novel catalytic compounds [5–7]. To date, three general types of approaches have been utilized for the analysis of combinatorial libraries of heterogeneous catalysts. The first approach is to implement currently available “one sample at a time” techniques, such as mass spectrometry (MS) or gas chromatography, and combine them with multiple-well reactors and switching devices. These approaches are the easiest to implement with a small number of samples. It is, however, apparent that this method will consume too much time when large catalyst libraries are screened, since the screening time is directly proportional to the number of samples to be analyzed. The second analytical approach is based on the modification of conventional serial techniques using automation approaches in order to decrease the screening time. Amongst these are scanning MS [8–14], gas chromatography [15,16], gas sensors [17], and resonance-enhanced multiphoton ionization [14,18]. All of these methods take advantage of the ability to run reactions in a parallel fashion, but the testing is still performed in a sequential manner. At this stage, high-quality data are often sacrificed for improved speed by compromising the catalyst testing (e.g., evaporated mixed metal libraries on flat substrates, flowing gases over catalyst powders instead of plug-flow geometry) and therefore make accurate evaluation of catalyst performance very difficult. Again, the screening time is directly proportional to the number of samples to be analyzed. The third approach involves truly parallel screening techniques, which gather data simultaneously from all catalysts in a library under realistic conditions. This category includes infrared thermography, fluorescence imaging, and FTIR imaging. IR thermography detects infrared radiation emitted by objects and has been used to detect activity for exothermic reactions in combinatorial libraries in a truly parallel fashion [18–21]. Thermal imaging does not, however, possess any ability to chemically resolve product composition. Therefore, it is not clear whether any apparent “activity” observed is due to the desired reaction or unexpected side reactions. This is a key issue in studying complex reactions using supported catalysts and highlights the necessity to gather chemically specific information about products from each library member. Laser-induced fluorescence imaging relies on a fixed laser wavelength exciting fluorescence in molecules. The laser excites both products and reactants above the catalyst library during testing and this technique is limited to detecting molecules that fluoresce. The technique measures relative activity changes among a group of catalysts and is not truly quantitative [21,22].

Thus, most analytical techniques currently used for HTE of catalysts have been developed for rapid screening of relative activity and are not capable of truly quantitative measurement of catalyst performance. In order to advance combinatorial studies to the next higher level, we believe that the analytical techniques must give quantitative data. FTIR imaging is the only quantitative, chemically sensitive, and parallel HT technique that has been reported to date. Over the past three years, we have demonstrated that this technique can be successfully applied to the screening of a variety of combinatorial systems [23–25]. FTIR imaging is a technique that couples a focal plane array (FPA) detector with an FTIR spectrometer to enable the simultaneous collection of spectral and spatial information [26]. In FTIR imaging studies, spectral information is collected from regions of a sample in order to study its spatial and chemical heterogeneity. Conversely, the basic concept of the application of FTIR imaging to the analysis of combinatorial libraries is to place many samples in the field of view of the instrument in order to analyze them simultaneously [27]. This provides a multiplex advantage, in which chemically specific information is collected from multiple samples during a single experiment. Our current setup allows us to take IR spectra with spectral resolution 8 cm^{-1} of the effluent of 16 supported catalyst samples in parallel every 1.5 s. The catalysts are arranged in a plug-flow reactor configuration, which facilitates a 15-min changeover of all samples, and the temperature of each catalyst is measured by individual thermocouples located in the catalyst bed. This setup provides us with the possibility to quantitatively study steady state and transient phenomena on combinatorial libraries.

Figure 3 displays the relative CO_2 concentrations in the effluent of 16 reactors during CO oxidation over transition metal catalysts on γ-Al_2O_3 and SiO_2 supports. The information on catalyst performance is obtained by fixing the image frequency on a spectral feature of interest, in this case one

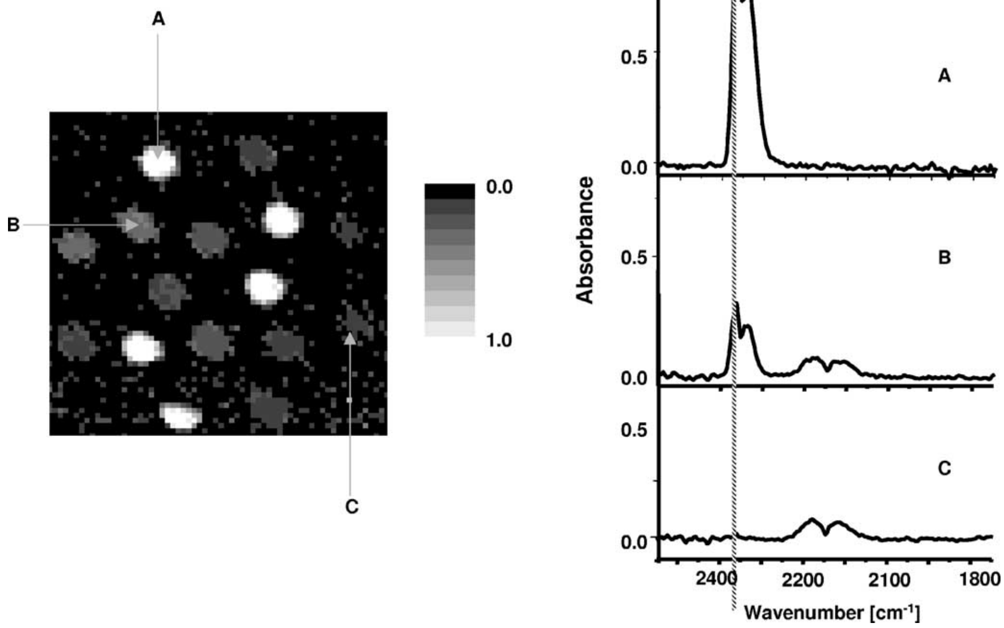

Fig. 3. Image of the gas phase array showing the absorbance intensities at 2364 cm^{-1} as varying grayscale levels corresponding to the effluent concentrations of CO_2. Spectra A, B, and C have been extracted from the positions indicated in the image. Spectrum A shows an active catalyst (high CO_2 concentration). Catalyst C has no CO_2 peak and a CO peak, indicating that this catalyst is not active under the applied conditions. The activity of catalyst B lies between those of catalyst A and C.

vibrational branch of gas-phase CO_2. The grayscale level indicates the extent of CO oxidation, light being high CO_2 production and dark being low CO_2 production. Thus, we obtain instant information about the activity of all library elements. FTIR imaging has of course the same quantitative abilities as single-element FTIR spectroscopy, where IR absorbance can be directly related to the concentration [28]. The quantitative capability of FTIR imaging becomes very important when not only a rapid activity screen will be applied, but quantitative information, such as turnover frequencies, concentrations of individual products, and material balances are important; i.e., it is essential for the knowledge extraction we envision.

We have used FTIR imaging to obtain reaction orders for a library of 16 different supported catalysts. The CO partial pressure was varied while the O_2 partial pressure was kept fixed. The reaction was carried out at ambient pressure and He was used as the diluent. Gas-phase IR spectra under different steady-state conditions were analyzed for each of the catalysts by integrating the CO and CO_2 IR-absorbance-band area, and calibration curves allowed conversion of the peak area to partial pressure. Figure 4 shows a log–log plot of the reaction rate vs CO partial pressure for Pt, Rh, and Ru, which all were supported on γ-alumina. The slopes indicate the CO reaction order. Having nine of these reactors loaded with three different amounts of each type of catalyst gave immediate information on the absence of interparticle mass transport limitations and ensured that only data in the differential regime were considered for each reaction condition. The carbon balance was readily closed on each reactor, and activation energies were obtained from steady state measurements at five temperatures—less than 2 h work for 16 catalysts. Activation energies and materials balances can be obtained. All these quantitative data can now

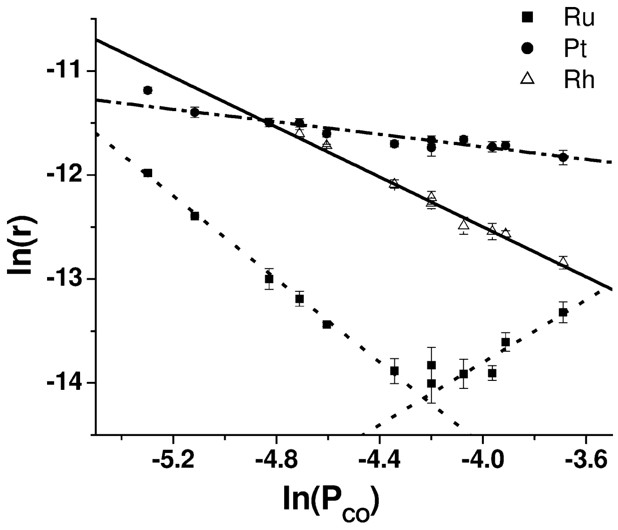

Fig. 4. Order of reaction plot of $\ln(r)$ vs $\ln(P_{CO})$. The two lines through the Ru data points represent a change in the reaction order with CO partial pressure.

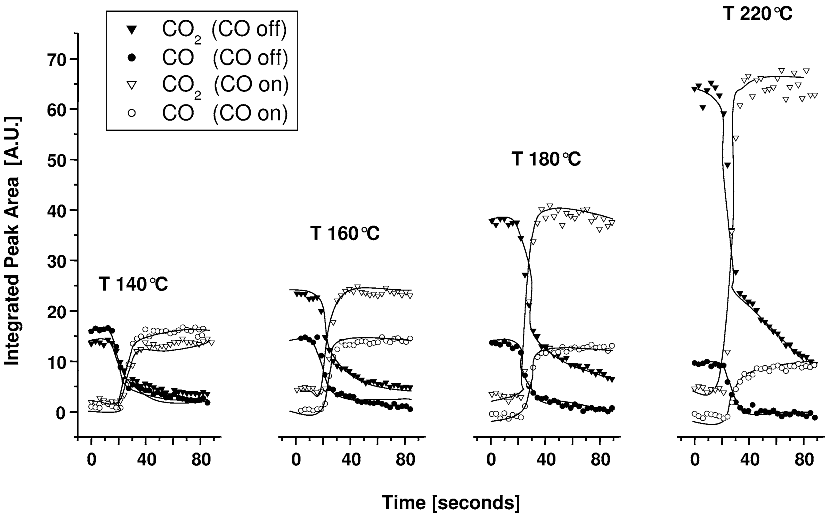

Fig. 5. Integrated absorbances for the CO and CO_2 bands for experiments in which CO is turned on (open symbols) and off (filled symbols) in a steplike fashion in a constant stream of oxygen and helium. Lines are drawn through data points for visual clarity.

serve as high-quality input for the modeling framework to be described in this paper.

The speed of FTIR imaging also enables us to follow transients during reactions. Transient behavior of catalysts and insight into the underlying non-steady-state kinetics are relevant to many catalytic systems. This applies, for example, to any system where the catalyst is periodically regenerated or where cyclic feed and other measures are being taken to force a chemical reaction. It can also extend the sampling space for validating kinetic models. Figure 5 shows transient data for CO oxidation for one of the 16 reactors. The data are collected every 3 s over a period of 90 s. The transients show the response of this particular catalyst to step introduction of CO in the feed and then to CO shut-off with continuously flowing oxygen and helium. These step changes are repeated for four different reaction temperatures between 140 and 220 °C. The response is shown in changes in the CO and CO_2 partial pressures in the reactor effluents. This type of transient data are collected simultaneously for all 16 reactors and the whole experiment was carried out in less than 1 h. The transient data show, as expected, that with increasing temperature the CO conversion increases. More interesting are the changes in the CO_2 response. At lower temperatures the CO on/CO off responses are mirror images of each other, but as the temperature increases a difference between the two becomes apparent. This result points towards storage of carbon on the catalyst surface, possibly as a carbonate or carbide as the temperature increases.

3. Knowledge extraction

3.1. Overview

In order for quantitative HTE to reach its full potential, KE must occur at a rate that is comparable to the ever-increasing rate of data generation. In this section we will describe a specific, computer-based, KE engine that will work in concert with a human expert in development of a forward model. The key concept is that the computer-based KE engine should approach data and models in a similar manner as that used by the human expert. It is important to realize that data are information, not knowledge, and while multicolor and 3D visualization may allow one to better observe the data, the real objective is to capture the knowledge content of the data in a form that allows continuous accumulation of knowledge. A computer-based system will never be able to fully capture the rich thought process of a human expert, but neither can the human expert alone handle the flood of data from HTE and the range of predictions possible from ever more sophisticated models. It is our hypothesis that the combination of a computer-based KE engine in concert with a human expert is needed.

A schematic of the KE engine for the kinetic model is shown in Fig. 6. Both HTE data and chemistry rules

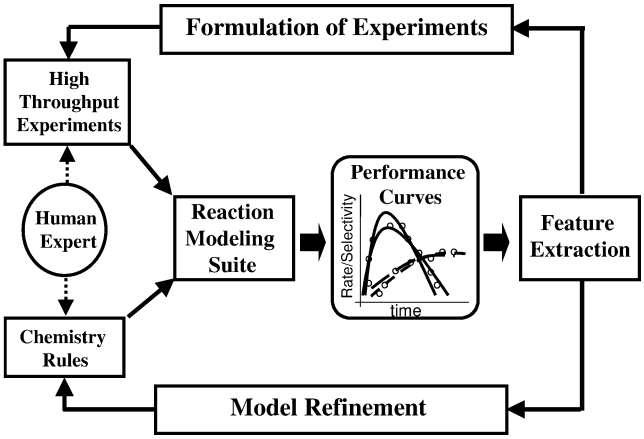

Fig. 6. Schematic of the knowledge flow in a knowledge extraction engine for the kinetic model.

are the starting point, models are automatically generated from rules, the parameters of the model are optimized by comparing the predictions of the model with the data, and finally the features of the predictions and data are compared. For example, in the simple catalytic reaction A goes to B, the "rule" that A must be adsorbed reversibly leads to the "feature" that the rate of production of B will show a maximum with increasing temperature. To build the kinetic model one should *first* decide on how knowledge should be represented. In our opinion, the human expert does not primarily think in terms of the detailed mathematical formulation of a model; rather he or she thinks in terms of the "rules" that lead to that model. The analysis of predictions vs data, at least during the early stages of model development, is not primarily via a least-squares fit, but rather through a comparison of the "features" of the data vs those of the model. Thus, a KE engine for model development should be able to map "rules" to "features" accurately, robustly, and automatically. *Second*, the best human experts are very good at Model Refinement by at least partially solving the inverse feature-to-rule mapping, i.e., changing the rules to improve the features. Thus, the development of automatic, computer-based algorithms to address the very difficult inverse feature-to-rule mapping will be essential. *Third*, since at the onset the data may be compatible with several potential models and there may be multiple parameter sets for each model (i.e., the models are nonlinear), the KE engine will need to help formulate new, critical HTE experiments that will discriminate between the models and parameter sets. *Finally*, as shown in Fig. 6, KE is not a one-pass process—it is cyclic. If the KE engine in concert with the human expert works effectively, *convergence* of model predictions with the data should eventually occur, resulting in a robust forward model.

3.2. Review of knowledge extraction for chemically reacting systems

The most comprehensive approach to date for catalytic performance is the MicroKinetic (MK) approach of Dumesic and co-workers [29]. Although reaction network analysis predates the MK approach by several decades [30,31], MK analysis is a systematic approach to heterogeneous catalysis that uses a wide range of experimental and theoretical information to test various model hypotheses. Applications of the MK approach include detailed reaction analysis on metal, oxides, sulfides, and zeolites [32–37]. MK analysis has provided considerable insight into the fundamental behavior of catalytic systems; however, in its current form knowledge extraction via MK analysis is inexorably tied to a level of human intervention that is incommensurate with HTE and the increasing complexity of fundamental models.

Computer-generated development of large-scale reaction mechanisms has been used extensively in hydrocarbon combustion, oxidation, and pyrolysis [31,38–47] and organic synthesis [48–51] modeling. These efforts include the representation of reaction species and pathways using matrices [39,44,46], structure-oriented lumping [52,53], optimization, and statistical analysis [54–58]. Of particular interest are the work of Mavrovouniotis and Prickett [59–61] in developing a compiler for generating chemical reactions from chemical rules, a graph-theoretic method to identify candidate mechanisms [62], and recent work by Koza et al. [63] using genetic algorithms to discover potential reaction pathways. The reaction network is often pruned using a variety of techniques [54,64,65], including sensitivity analysis [54–57, 65–67], math-programming methods [45,68–70], and manifold techniques [71,72]. However, these methods depend upon the elimination of species and/or kinetic steps that are not important for a particular data set, where there is no assurance that this species and/or reaction mechanism will not become important for other reaction conditions. In contrast, Mavrouvouniotis and Prickett [59] suggested model reduction methods where known reactivity relationships between different species are used to eliminate unimportant reactions, or alternatively reaction-rate-based techniques have been used to control the size of the network [73]. The tools described above are certainly essential components of any computational approach to catalyst design; however, these tools only facilitate the implementation and fitting of models, not the automation of deep reasoning.

Because of the complexity of predicting catalyst performance, several AI methods have been applied to this problem. Complex systems that are not amenable to detailed first-principles modeling can be described via artificial neural networks (ANN). For example, ANN have been developed to explain performance of a catalyst on the basis of its structure and other descriptors [74,75]. Two major disadvantages of ANN are that they need large numbers of training data and that their predictions beyond the domain of the training data are poor. These drawbacks have been addressed by hybrid neural networks [2,76–80] that use first-principles knowledge with an ANN. The idea of using qualitative reasoning was demonstrated by Banares-Alcantara et al. [81,82] in an expert system for catalyst selection. Hattori et al. [83] report a knowledge-based system for designing catalysts based on information about catalyst activity patterns. McCleod and Gladden [84] have used a stochastic optimization algorithm to optimize the geometric arrangement of the catalytic sites that maximizes the catalyst activity. Recently Baerns and coworkers [85,86] demonstrated an evolutionary approach to combinatorial selection and optimization of catalytic materials. Their methodology uses genetic algorithms to guide combinatorial experiments in a search for catalysts. The objectives of the methods described in this paragraph are to model data and find new catalytic materials; however, these AI approaches do not directly address how an improved understanding is to be developed.

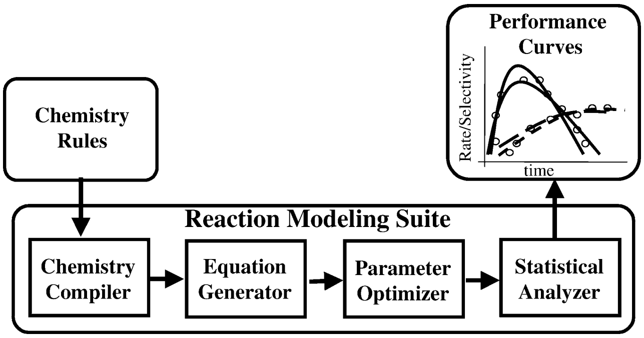

Fig. 7. Schematic of the various tools in the reaction modeling suite.

3.3. Knowledge extraction—rate constants to performance

We will now discuss a potential framework for KE for the kinetic model. The first component of the KE engine is a set of tools for generating model predictions of kinetic performance from chemistry rules and experimental data. As shown in Fig. 7 this set of operations include (i) translation of chemistry/catalyst rules such as basic reaction pathways, postulated groupings of species with similar reactivities and Polanyi relationships, written in near-English language form to a computer compatible syntax, (ii) generation of the appropriate algebraic and/or differential equations (DAEs) consistent with the rules, (iii) solution of the DAEs with minimal user intervention including nonlinear optimization to determine the sets of model parameters that can best fit the data either via least squares or in terms of features, and (iv) statistical analysis of the various fits. Because the models are nonlinear and the data are often incomplete or noisy, there may be many parameter sets for a single model and/or multiple sets of rules that can describe the data. Consequently, the analysis process must be extremely fast, robust, and inclusive if it is to keep up with the speed of HTE. We have recently developed a genetic algorithm (GA)-based optimization procedure [87] that is able to locate large numbers of local minima that are nearly indistinguishable from the global minimum at a rate that is at least two orders of magnitude faster than alternative search procedures [88]. This allows a more complete evaluation of all the parameter sets consistent with a given data set, rather than just choosing between the first several parameter sets that fit the data.

Application of the kinetic modeling tools as they currently exist is illustrated for the problem of production of aromatics from propane using H-ZSM-5. A number of kinetic models have been proposed for aromatization of alkanes over ZSM-5 [89–91]; however, a model with predictive capabilities remains a challenge. Our kinetic model is based on a reaction scheme involving adsorption, desorption, protolysis, dehydrogenation, hydride transfer, β-scission, oligomerization, and aromatization reactions. The proposed set of reaction “rules” generates a very large number of individual reactions. To reduce the number of parameters involved, the reactions were categorized into various families and all reactions in a particular family were assumed to have the same rate constant or a set of rate constants that are a specific function of the carbon number of the species. The model consists of 31 gas-phase species, 29 surface species, and 271 reaction steps, which have been categorized into 33 different families. Each reaction family is parameterized in terms of either a rate constant or an equilibrium constant and the carbon number dependence within a family is considered in terms of the Polanyi relation. Transition state theory has been used to estimate bounds on the preexponential factors and literature values have been used to bound the activation energies [92–96] and provide interrelationships between various reaction families [97,98] to reduce the number of parameters to 13. The proposed model assumes that the reactions of neutral surface alkoxy species [94,99,100] take place through carbenium/carbonium ion transition states.

The results of the GA-based hybrid search methodology described above are presented in Fig. 8, where the data are taken from Lukyanov et al. [91]. The results of local sensitivity analysis for the optimal parameter set are given in Table 1, where 7 of the 13 parameters are particularly sensitive for modeling the data. We also located 32 additional local minima that are almost as good with respect to the sum of squares error criterion. It is important to know if there are multiple local minima each with its own parameter set, since different minima can have different physical implications. The speed of the new GA-based hybrid search method allows more complete exploration of the global parameter space, which has obvious implications for assessing the validity of a given model.

The suite of modeling tools described above begins to allow more efficient handling of HTE data; however, it is not an automated KE engine, since there is no (i) mechanism for resolving discrepancies between the data and model by modifying the chemistry rules or (ii) help in the selection of new HTE experiments. A first step toward KE is the development of an automated process for identifying “features” of the data and predicted performance. Especially during the early stages of model development, the best least-squares fit to the data may in fact be a poor indication of model. Moreover, in diagnosing problems in the model, especially for multiple products as shown in Fig. 8, it is often more important to fit some parts of the data well (e.g., the initial region of the response), forcing the difficulties into areas that then can be more clearly evaluated. A feature vector is constructed by first defining a sequence of intervals that are separated by abrupt changes in the magnitude, slope, or curvature for either data or model predictions. The shape (e.g., linear, concave upward, etc.) is then defined for each interval. Each element in the feature vector now includes the location of the interval, shape, and least-squares fitting information if desired. The data can be optimized via traditional least-squares methods or alternatively on the features.

Once features of various potential models and/or parameter sets have been identified, model refinement is employed, which requires determination of the mapping between features and rules. Consider the case of developing a predictive

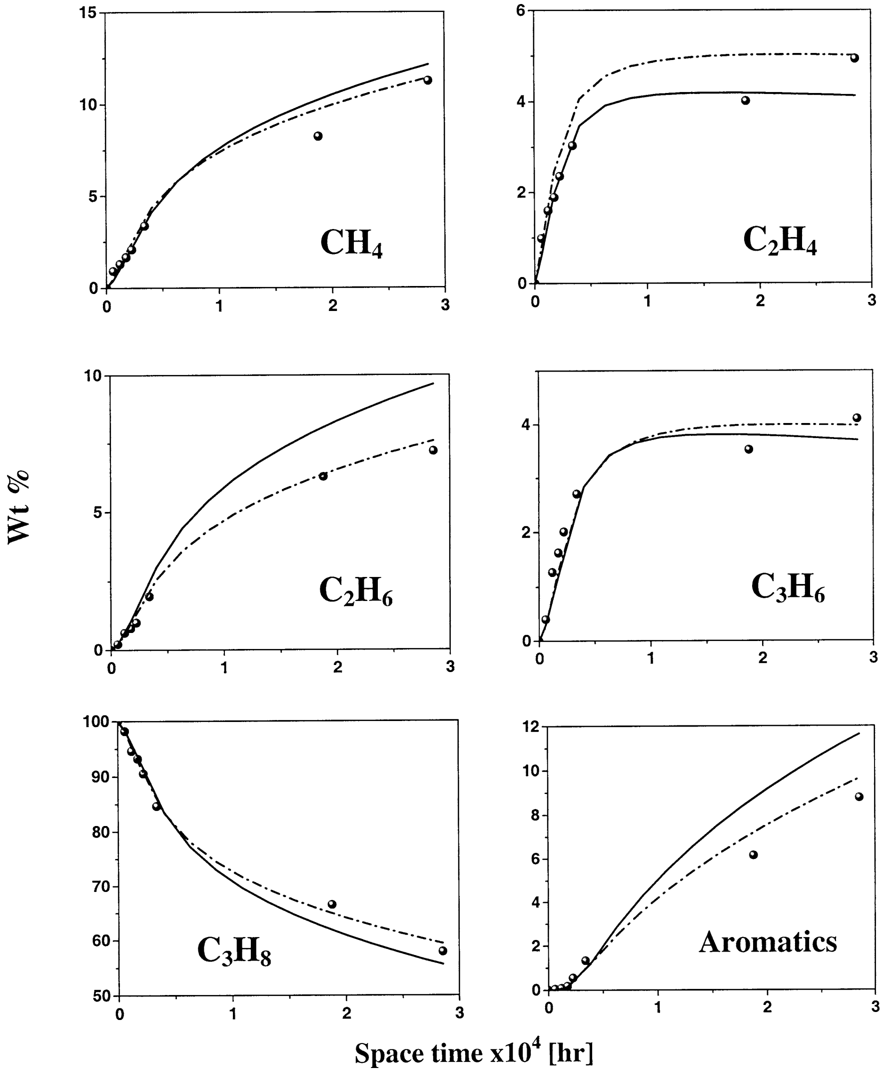

Fig. 8. Improvement in performance curves for propane aromatization on HZSM-5. Dots correspond to experimental data from Lukyanov et al. [91]; solid lines indicate the original model predictions and the dashed line indicate the refined model predictions. The x-axis is in terms of the space-time $\times$ 10^4 (h) and the y-axis is the weight percentage of the various species.

model for the data shown in Fig. 8, where a difference in feature (e.g., the magnitude of ethane production at high spacetimes) is observed between the predictions and data. These features were determined from an approximate set of rules, which were initially down-selected from a much more comprehensive set of rules for the carbenium ion chemistry of zeolites—i.e., the human expert made initial choices about what was important. A variety of alternative rules were then stochastically probed for their effect on light paraffin production. The most effective single rule addition was alkylation of alkoxy species with light alkanes [101,102]. This expanded rule set better captures the performance of the catalyst for all species. Thus, the inverse feature-to-rule mapping has determined what rule was needed from the global rule set using a stochastic search guided by expert information. Specifically, the human expert made a very reasonable, but incomplete, initial guess to start the process, and then the KE engine determined an improved rule set with associated kinetic parameters—i.e., KE has been achieved. A search over all possible sets of rules is impossible due to the significant computational demands of the forward rule-to-feature mapping and the combinatorial explosion if all rule combinations are considered. In this case, the solution was relatively straightforward, since the changes were localized around rules directly connected to the C_2 chemistry; however, there will be cases where changes would be needed in the reaction network that are not directly connected to the region of data/model feature discrepancy. The example outlined above should clearly shows the general principle behind model refinement, although considerable research remains to be done.

Although we have not as yet implemented an automatic algorithm for the formulation of experiments portion of the kinetic model shown in Fig. 6, we will briefly outline what we believe will be needed. As shown in Table 1, there may be multiple sets of kinetic parameters that can

Table 1
Results of nonlinear parameter estimation

S.no.	Model parameters	$\log_{10}$(value)
1	k_p	7 ± 7
2	k_{od}	4.5 ± 2.9
3	k_{ad}	9 ± 5
4	k_b	5.2 ± 2.4
5	k_a	7 ± 8
6	k_{aa}	1 ± 2
7	k_h	2.0 ± 0.7
8	k_{oa}	3 ± 2
9	k_{cd}	2 ± 2
10	Δq_{od}	0.77 ± 0.12
11	Δq_{ad}	1.1 ± 0.2
12	Δq_{cd}	0.3 ± 1.6
13	S	1.25 ± 0.01

Error in parameters obtained from the local sensitivity of the objective function to the parameters corresponding to the best minimum. Model parameters are rate constants for protolysis, k_p; olefin desorption, k_{od}; alkane desorption, k_{ad}; β-scission, k_b; aromatization, k_a; alkane adsorption, k_{aa}; hydride transfer, k_h; olefin adsorption, k_{oa}; carbonium ion dehydrogenation, k_{cd}; increase with carbon number of adsorption enthalpies for olefin adsorption, Δq_{od}, and alkane adsorption, Δq_{ad}; increase with carbon number of activation energy for carbonium ion dehydrogenation, Δq_{cd}; and the entropy change for the β-scission/oligomerization equilibrium constant, ΔS. First-order rate constants (k_p, k_{od}, k_{ad}, k_b, k_a, k_{cd}) are in terms of mol/g/h; second-order rate constants (k_{aa}, k_h, k_{oa}) in m^3/g/h; energy terms (Δq_{od}, Δq_{ad}, Δq_{cd}) are in kJ/mol; and the entropy term, ΔS, has been normalized by the universal gas constant (J/mol/K).

provide an equivalent description of the features of a given data set as quantified by the sensitivity matrix for the kinetic parameters. For a given catalyst system the features directly depend upon the feed composition and reaction temperature. Thus, one needs to develop algorithms similar to the model refinement procedure for guiding the inverse sensitivity matrix to reaction/feed dependence mapping in order to determine what type of HTE experiments will be most discriminating. This inverse search procedure may need to be extended to also include multiple rule sets as well as multiple sets of kinetic parameters for a given rule set. In this section we have summarized our work on development of an automated KE engine for the kinetic model. Considerable research remains, but we believe that the basic knowledge architecture is relatively complete. The key postulate in the development of the proposed architecture is that the software must capture the type of thought processes currently employed by the human expert.

3.4. Knowledge extraction—catalyst chemistry model

The problem of relating catalyst microstructure to rate constants is the next step in developing an overall catalyst design system and represents arguably the most challenging part. Our development of the catalyst chemistry model is much less complete than that of the kinetic model described above, but we believe that the basic organization of the catalyst chemistry model is reasonably firm and should provide a blueprint for future development. The input to the catalyst chemistry model is experimental data from the catalyst library and chemistry rules, working in concert with the human expert. These data and rules are used to determine a set of catalyst "descriptors" that define the important processes that control how the catalyst microstructure is connected to the reaction mechanism and rate constants. The aim of catalytic descriptors is to provide well-defined terms that capture the collective influence of microstructure on relevant kinetic model parameters. The identification, calculation, and subsequent refinement of an appropriate set of descriptors is the key task in development of the catalyst chemistry model.

Various methods can be used to provide the link between catalytic descriptors and kinetic parameters. For instance, a descriptor in zeolite chemistry could be the *Si/Al ratio*, which is correlated with acid strength and the proximity of acid sites. Other descriptors such as proton affinity [103] and deprotonation energy and chemical reactivity measures such as Fukui functions [104], hardness and softness [105], electron-sharing indices [106], electron localization functions [107], and local isoelectronic reactivity [108] may be useful; however, these descriptors lack a direct computational link to kinetic parameters. Examples of descriptors that do provide direct links to parameters include transition state geometries and activation energies, which are calculated using density functional theory; alternatively, a less direct means of rate constant estimation can be achieved by calculating heats of reaction and invoking the Brønsted–Polanyi relationships that relate activation energies to heats of reaction [109,110].

During the early stages of the KE process, a single descriptor may not provide a direct correlation between the catalyst microstructure and the kinetic parameters. At this point a hybrid model that relates a set of descriptors constrained by expert rules and guided by experimental data can provide a viable initial model. We have developed software where a neural network with multiple inputs is constrained by (i) equality and/or inequality constraints consistent with the chemistry rules and (ii) the complete or partial form of a fundamental model. As an example of the power of this software architecture, consider the two-step catalytic reaction to produce C from A in which species A adsorbs molecularly. Assuming that the adsorption step is quasi-equilibrated and A_{ads} + site → C + 2 sites, the rate expression is of the form $r_c = k_2 K_1 P_A/(1 + K_1 P_A)^2$, where r_c is the rate of C formation, P_A is the partial pressure of A, and K_1 and k_2 are model constants. Reaction rate data over a limited range of pressures were generated from this kinetic expression, adding experimental noise as shown in Fig. 9. The data were first fit via just a neural network, where as expected the fit was reasonable over the range of the data but diverged significantly for pressures outside the data range. Next, the neural network was constrained by assuming that the reaction order was 1 ± 0.5—a reasonable constraint exposed from the rules. For this case there was little change in the predictions inside the data range, but

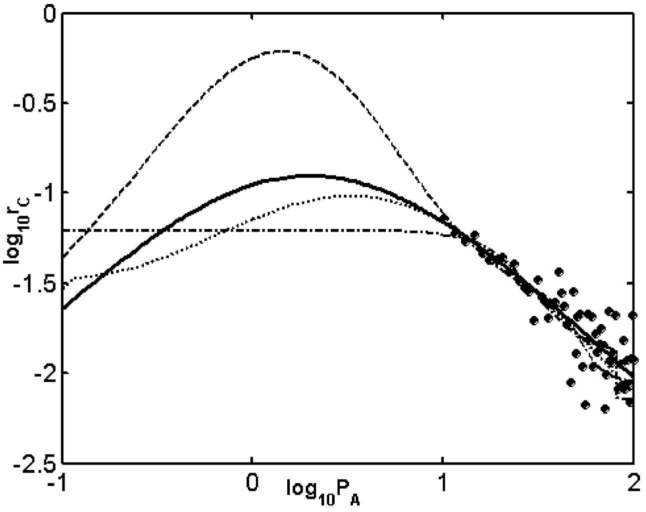

Fig. 9. Hybrid models for predicting performance from data and partial knowledge. Filled cicles indicate training data with noise; solid line indicates the true model; dashed–dotted line indicates the neural network predictions; dashed line indicates the predictions of the neural network where the reaction order is constrained to be 1 ± 0.5 and dotted line indicates the reaction order constraint of 1 ± 0.1.

extrapolation outside the data range was improved. Finally, the reaction order constraint at low pressures was tightened to 1 ± 0.1, and the hybrid model now did a much better job of extrapolation. This example clearly shows how a hybrid neural model with constraints from expert rules and first principles information can improve predictive capabilities as additional, but still perhaps incomplete, knowledge is added to the model. Unlike previous efforts at incorporating first-principles knowledge into neural networks [76–79], this architecture is truly parallel.

4. Summary

High-throughput catalytic experiments are changing the catalysis research landscape. While the number of catalysts in a library, the control of the catalytic environment, and the quantitative accuracy of the performance data continue to evolve, it is already possible to get a full set of concentration- and temperature-dependent data on 16 or more catalysts in less than a day. The speed offered by imaging FTIR detection even enables parallel quantitative transient analysis on the timescale of seconds. Consequently, more exhaustive searches of composition space and the close interplay of hypothesis and testing on reasonable time scales are now possible. These tools will certainly accelerate Edisonian discovery of new catalysts and also the generation of new understanding by the classical scientific method. What new opportunities do they afford? Even when an Edisonian search is successful, how can the information on both successful and unsuccessful catalyst formulations be converted to knowledge that will guide the next search? For complex catalytic systems driven by many interrelated and often hidden variables, are there tools that will help an expert discover the important relationships and arrive more efficiently at the research target? In this paper we have advanced the premise that model building is the key to knowledge extraction from the high density of information enabled by HTE. The model archives relationships between catalyst properties and performance, creating an ever-growing knowledge bank. The requirement that the model predicts performance quantitatively challenges the model structure and forces model components to capture fundamental relationships.

For this approach to be effective, model building cannot be the limiting step. Our reaction modeling suite affords a rational, automated framework that is designed to allow the expert to initiate the modeling sequence in a simple reaction chemistry language. The software then interprets this information into a reaction sequence, writes the appropriate equations, optimizes the fitted parameters while keeping parameters in physically and chemically allowed bounds, and does statistical analysis of the results. These steps have been fully demonstrated in the propane-to-aromatics example in the text above. The genetic algorithm approach to parameter estimation is of particular note, since it enables thorough search of the parameter space with a dramatic improvement in speed over other methods.

It is a rare event for an initial kinetic model to be thorough enough to fit all the data, so it is essential that the modeling approach also facilitate model refinement. We have focused on feature identification and the mapping of features to reaction rules as an efficient path for model improvement. The concept has been demonstrated on an example problem. A key element of this aspect of the model building is that, as shown schematically in Fig. 6, iteration of model comparison to high-throughput data and subsequent model refinement lead to *convergence* to a predictive kinetic model. Thus, the goal of the reaction modeling suite is to facilitate MK analysis—but this is only one part of the *forward model*. The catalyst chemistry part of the model calls for identification of chemical descriptors and the mapping of the descriptors to the kinetic model and its parameters. We have outlined approaches that will enable this step but we appreciate its difficulty. We will rely on the iterative convergence implied by Fig. 6 to carry us from crude initial models to increasingly sophisticated ones, and we expect this process, although probably slow, to strengthen our understanding of the fundamentals of catalytic behavior. This opportunity for model evolution arises from the ability to construct hybrid software architectures that mix first principle, data driven and expert rule models. During the initial stages of the KE process, the data may carry most of the predictive load, while after multiple passes through the KE engine more fundamental models will carry more of the predictive load and thus have more robust extrapolation capabilities.

A successful forward model has considerable value in its own right, but its power is dramatically leveraged by the *inverse model*, which forecasts catalyst formulations that will solve targeted problems. This potential to truly design catalysts is the return on the investment in model building. Because of the complexity of the problems, knowledge extraction in the model can only be driven by large amounts of high-quality data; i.e., KE relies on HTE and vice versa.

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