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Finding physical insights in catalysis with machine learning

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Machine learning (ML) has emerged as an invaluable approach for deriving predictive models in the catalysis field. While they are successful in making accurate predictions, many ML models are complex and difficult to interpret. In this opinion, we discuss recent progress in the development of *explainable* ML models in catalysis. In particular, we focus on the prospect of using symbolic regression (SR) to derive physical models that are based on analytical functional forms rooted in fundamental physics. We overview the basic concepts underlying two popular SR methods (genetic algorithms and compressed sensing), as well as provide recent examples of their application in the catalysis literature.

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Introduction

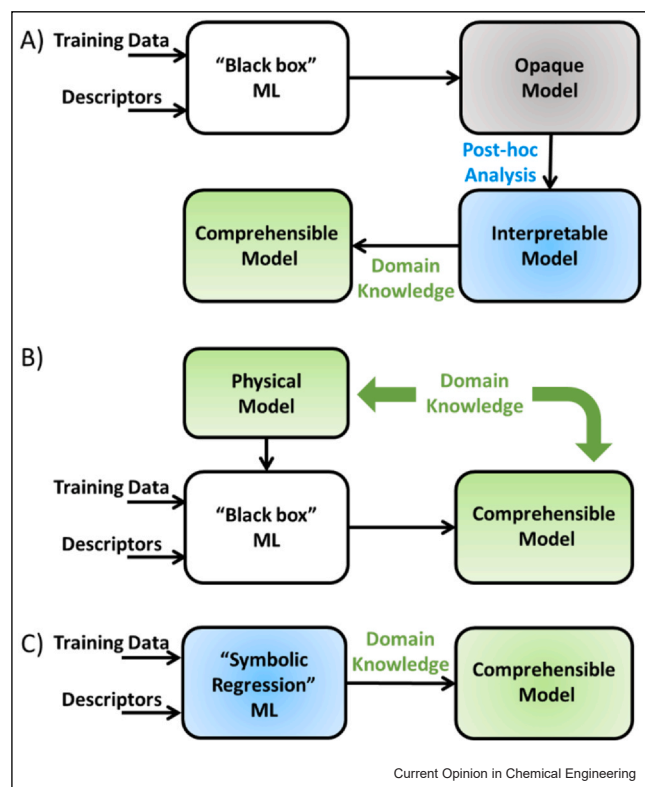
When we deeply understand a physical process, we can distill the salient features of that process into property descriptors that dictate the behavior of the system. In other words, we understand how to build a functional relationship between a system's properties and its observed behavior. We refer to these relationships as *models*, *theories*, or *laws*, depending on their degree of generality and on our confidence in the observational data that support them. Traditionally, constructing these relationships requires careful analysis of data and logical application of physical insight on the part of the scientist. However, a new paradigm is emerging enabled by

the flood of accessible data and computational resources available to interrogate that data with statistical rigor. Machine learning (ML) can use these data to predict system properties with high accuracy and is finding increased relevance in the chemical engineering discipline [1]. The prominence of ML in the catalysis field is growing, as illustrated by several recent reviews and perspectives of ML-guided catalyst design [2–6]. ML models have been used in many studies as a way to efficiently screen materials space for desirable catalytic properties [7–13]. However, the models generated in these studies are often complex and thus become ‘black boxes’ that are difficult (but not impossible) to interpret. Indeed, there is a well-known trade-off between model simplicity and model accuracy. Simpler models are easier to interpret and can usually describe qualitative behavior, but they often fail to meet requirements for quantitative accuracy. On the other hand, complex models achieve high accuracy at the expense of interpretability. Several researchers are working to break this trade-off by developing methods for deriving *explainable* ML models relevant to catalysis [14]. Here, we classify the taxonomy of model *explainability* using three classifications defined by Doran et al. [15]:

- (1) Opaque model: A model that makes useful predictions but provides no further insight.
- (2) Interpretable model: A model that makes useful predictions and tells us which inputs most heavily influence the predictions. Functional relationships between the model inputs and the predicted outputs are known, but the physical principles underlying these relationships are not known.
- (3) Comprehensible model: A model that makes useful predictions and the functional form of the model can be derived from fundamental physical principles, or first principles.

In this opinion, we explore model explainability in catalysis. In particular, we will focus on the prospect of using ML to construct *comprehensible models* for catalytic systems that can be related to foundational physical principles. We will not review all of the strategies for enhancing model interpretability that have been developed in the catalysis field, but we will briefly highlight some of these strategies. For a more complete review of

Figure 1



Various strategies for deriving comprehensible models. (a) Interpret opaque models with post-hoc analysis and domain knowledge. (b) Incorporate physical models and domain knowledge upfront to derive theory-infused models. (c) Apply symbolic regression and domain knowledge to identify known or new physical models.

the recent literature on interpretable ML in catalysis, we refer the reader to an excellent critical review by Xin and coworkers [4].

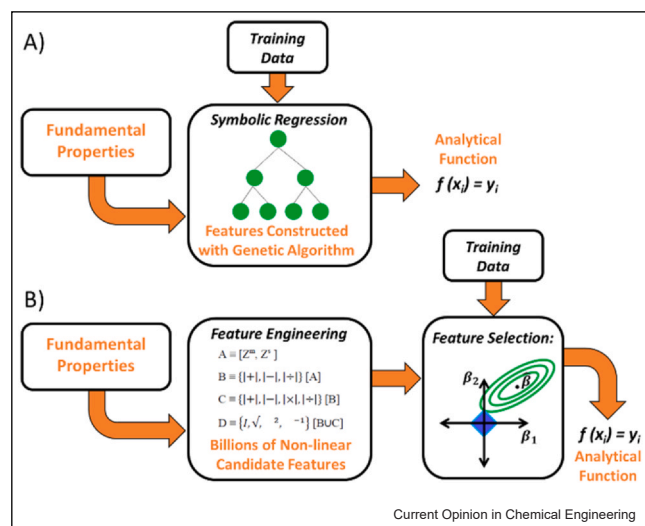
A few strategies for building comprehensible models are summarized in Figure 1. The first strategy shown in the figure uses post-hoc analysis to interpret otherwise opaque models derived from ML techniques such as deep neural networks (Figure 1a) [16]. At a high level, this strategy applies sensitivity analyses or feature-importance analyses to determine the input descriptors that exert the greatest influence on the model output, which has been demonstrated to yield deep physical insight in numerous catalysis studies [4,17–19]. Some ML methods are particularly amenable to interpretation, such as generalized additive models (GAM) that construct predictive functions composed of linear combinations of nonlinear operators acting on single physical descriptors [20]. Each operator in the linear combination acts on only one physical descriptor and, therefore, it is straightforward to identify which physical descriptors are most important and how they are functionally related to

the model output. For example, Esterhuizen et al. [21] used a GAM model to understand adsorbate binding on metal-alloy catalysts. Post-hoc analysis potentially can lead to comprehensible models if the resulting models are simple enough to understand completely with domain knowledge. Another strategy is to use known physical principles to build physics-informed, or theory-integrated, ML models (Figure 1b) [22,23]. For example, Xin and coworkers [24] demonstrated the development of a theory-infused neural network for predicting adsorbate binding on transition-metal surfaces, wherein d-band theory within the Newns–Anderson model is combined with deep neural networks. The resulting theory-infused model is fully comprehensible and can identify strategies for exploiting the known physics of chemisorption in unexpected ways. Of course, to implement this strategy, one must start with a known physical model, which is not always available. A final strategy is to employ ML methods that enforce interpretability by strategically limiting the complexity of model, which has the potential to generate parsimonious models that are comprehensible with the application of domain knowledge (Figure 1c). Though there are multiple strategies for constructing the model, we emphasize here that domain knowledge is always required to select and collect the primary descriptors. Here, we will overview this final approach, wherein symbolic regression [25] (SR) is the methodology used to learn analytical models. We will highlight examples from the literature showing how SR has the potential to lead to comprehensible models relevant to catalysis with limited amounts of data, given the difficulty of data collection in the catalysis and materials science fields.

Constructing models with symbolic regression

The goal of any ML procedure is to develop a function of the form $f(x_i) = y$, where x_i are known properties of the system and y is a property of interest. There are several approaches for building the model function f , such as using regression to identify the optimal parameters of a predefined functional form. The objective of SR is to construct f without imposing predefined functional forms [25,26]. Several algorithms have been developed to complete this task [27–30]. Two approaches we will discuss here are genetic algorithm [27] (GA) and compressed-sensing [31] (CS) methods (Figure 2). Other promising SR approaches are available, such as AI Feynman [32] and SR with Bayesian optimization [33], artificial bee colony [34], and deep learning [35], which have not yet been applied widely in the catalysis field. GAs build f by mating simple mathematical operators and analytical functions (Figure 2a) [27], where the best-performing functions of each generation are selected to parent the next generation to progressively build the complexity of the model's functional form. Random

Figure 2



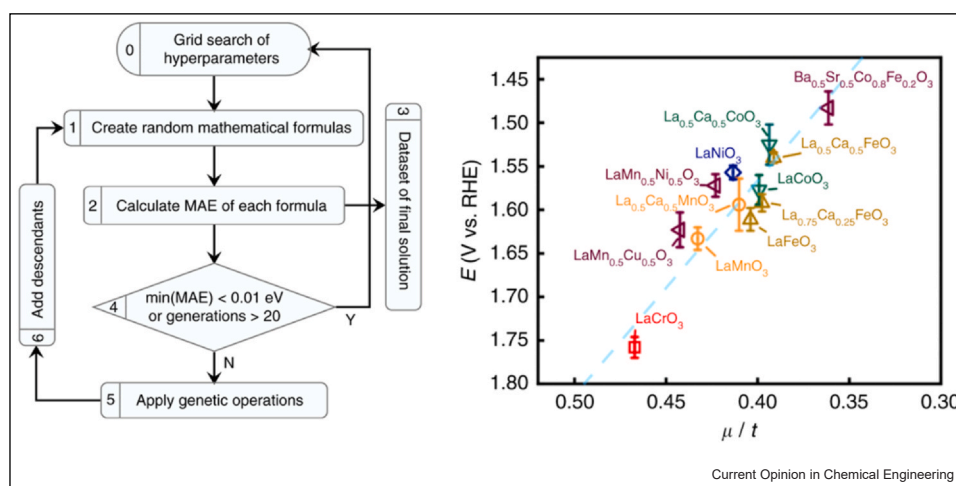
Symbolic regression workflows with (a) GA and (b) CS.

mutations are introduced to ensure that the algorithm does not become trapped in local minima. This method can potentially learn physical laws directly. Indeed, Schmidt and Lipson [26] showed that SR can be used to extract free-form natural laws from only experimental data. They demonstrated that GA–SR recovers the laws of classical mechanics using only experimental tracking data for chaotic pendulums. Their GA–SR algorithm had no *a priori* knowledge of physics, yet it was able to recover the Hamiltonian and Lagrangian functions that govern the system’s mechanics. Rondinelli et al. [27] advocate for the use of GA–SR as a means for deriving

physical laws in materials science. They show that GA–SR can rederive two well-known physical laws (i.e., the Johnson–Mehl–Avrami–Kolmogorov equation and Landau free-energy expansion) [27]. We are only aware of one study so far that has applied GA–SR to a catalytic system, which was reported by Weng et al. [36] (Figure 3). The authors synthesized 18 perovskites and measured their oxygen evolution reaction (OER) overpotentials, and then used GA–SR to derive a physical descriptor to then predict the overpotential. The resulting descriptor was simply the ratio of two structure factors, revealing that the catalytic activity of oxide perovskites is dominated by structural stability. This descriptor was then used to design better catalyst compositions, which indeed achieved higher OER activity than the original perovskites. This work shows how SR not only led to a practical descriptor for screening, but also provided important physical insight.

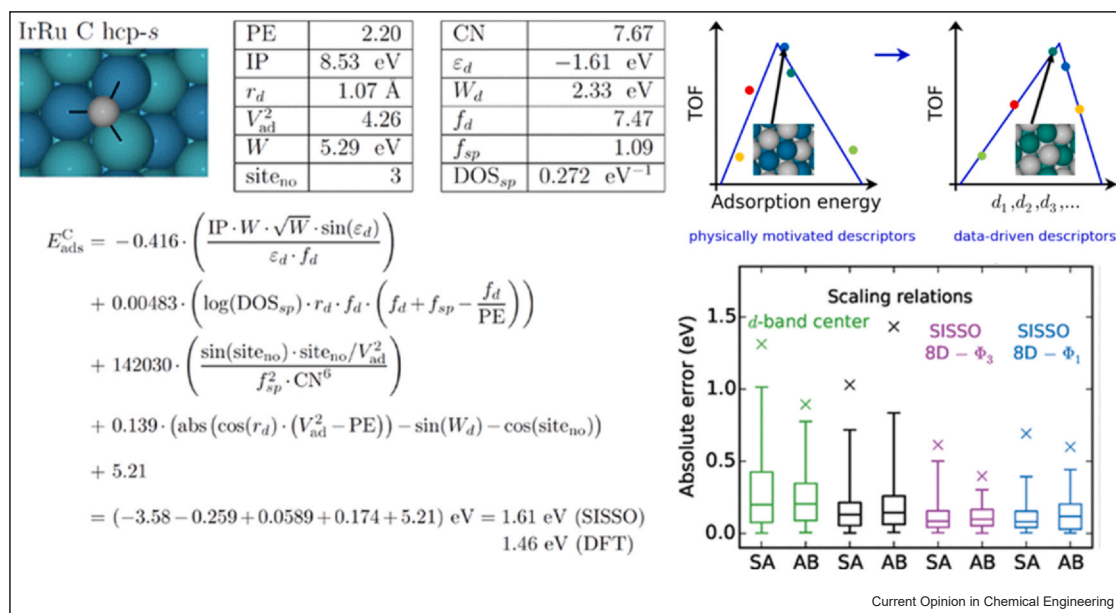
Another prominent symbolic regression method uses CS as a strategy for constructing the model function f [31]. GA–SR methods use directed evolution to progressively build complex functional forms. CS instead engineers a large candidate pool of functional forms and then uses training data to identify the strongest candidate descriptors in the pool (Figure 2b). This approach was popularized for materials discovery by Scheffler, Ghiringhelli, and coworkers, who developed the LASSO+ ℓ_0 [31,37] and SISO [38,39] methods. In this workflow, primary features, which are basic physical descriptors, are engineered by applying a recursive series of mathematical operators to populate a large candidate pool of complex features. This feature-engineering step produces descriptors that capture nonlinear dependencies that may link fundamental system properties to the

Figure 3



Symbolic regression workflow for deriving a simple physical descriptor for predicting OER overpotential of perovskite catalysts. Adapted with permission from Weng et al. [36] Copyright 2020, Springer Nature.

Figure 4



Andersen et al. use SISSO to discover improved descriptors in catalysis. The analytical functions derived by SISSO yield lower error than the physically motivated d-band center theory.

Adapted with permission from Andersen et al. [40] Copyright 2017, American Chemical Society.

predicted material behavior, as well as capture interactions between individual features by including multi-feature operators, such as differences and ratios. The final model is constructed by feature selection via a sparsifying operator (e.g., regularized regression) that identifies the optimal descriptors from the pool of candidates. This approach was applied to catalysis in a CS workflow adapted by Andersen, Reuter, and coworkers [40–43]. Their work shows how SISSO can derive data-driven descriptors that outperform some of the most well-known physically motivated descriptors (Figure 4). This work also demonstrated a path forward for systematically improving models by identifying perturbative corrections to known physical models and scaling laws, as demonstrated in Andersen et al. [40] for predicting adsorption energies on metals with the d-band model, in Sun et al. [44] for predicting CO₂ adsorption energies with a more accurate descriptor than the d-band model, and in Xu et al. [41] for predicting adsorption energies on oxides with adsorbate-scaling laws. In each case, close inspection of the SISSO models revealed strong physical motivations for the perturbative corrections, thus providing signposts for improving established theories. This approach has steadily grown in popularity and has been applied in numerous studies [45–50]. Our group has adopted a similar strategy in some of our studies and has developed variations in the approach to incorporate Bayesian principles [51–53].

Perspective and outlook

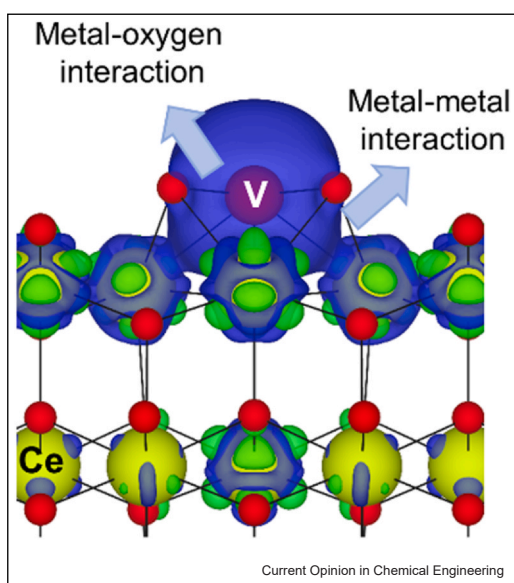
Can SR extract comprehensible models relevant to catalysis? The studies highlighted above suggest that the answer is yes, as they show that SR can recover descriptors related to known theories of adsorbate binding on metals and oxides. Some other examples from the literature show that CS can go beyond the descriptor level by arriving at analytical expressions that are similar in form to known physical models. For example, Hennig and coworkers [54] used SISSO to develop a physical model that predicts superconducting critical temperatures, where the newly derived model has a similar formulation to the Allen–Dynes equation. Some of our work has applied the CS strategy (O’Connor et al. [55]) to build models describing charge transfer between metal atoms and oxide surfaces, which has broad implications for controlling the activity and stability of single-metal-atom catalytic sites. We employed the LASSO+ l_0 workflow to derive models for predicting metal-atom binding on oxide surfaces (Table 1). Given the computational cost of density functional theory, we collected adsorption energies for only seven oxide surfaces and thirteen adsorbed metals, leading to a training set of 91 data points. Despite the modest size of the training set, the resulting model shown in Table 1 with one physical descriptor (1D) captures the main physics controlling the metal-binding energy. It is constructed from the metal adatom’s oxide-formation enthalpy

Table 1

Physical descriptors and predictive models derived from LASSO+ l_0 in O'Connor et al. [55]. Important terms are discussed in the main text and all terms are defined in the original paper.

	Predictive models for computing metal-binding energy on oxide surfaces	R ²
1D	$-0.15 \times CN_{bulk}^m \times \left \frac{\Delta H_{f,ox}}{\Delta E_{vac}} \right - 0.40$	0.95
2D	$-0.48 \times \sqrt{EA^m} \times \left \frac{\Delta H_{f,ox}}{\Delta E_{vac}} \right - 1.18 \times \left \frac{L^s}{L^m} \right \times \left \frac{\Delta H_{f,ox}}{\Delta E_{vac}} \right - 0.077$	0.96
3D	$-0.32 \times \sqrt{EA^m} \times \left \frac{\Delta H_{f,ox}}{\Delta E_{vac}} \right - 1.09 \times \left \frac{L^s}{L^m} \right \times \left \frac{\Delta H_{f,ox}}{\Delta E_{vac}} \right - 2.12 \times \left \frac{IE_2^m - IE_4^s}{IE_2^m} \right \times \left((\eta^m)^{\frac{1}{3}} - (\eta^s)^{\frac{1}{3}} \right)^2 - 0.32$	0.97

Figure 5



Computed charge-density difference of a V atom adsorbed on a CeO₂(111) surface, where red, green, and purple spheres represent O, Ce, and V, respectively. Green and blue represent electron-density depletion and accumulation, respectively. The isosurface level is $\pm 0.005 e \text{ Bohr}^{-3}$.

($\Delta H_{f,ox}$), which represents the interaction strength of the adsorbed metal and the surface oxygens [56], and the oxygen vacancy-formation energy (ΔE_{vac}), which represents the reducibility of the oxide surface. These two properties together can be used to predict charge transfer between the metal and the support, as the former predicts the ability of the metal to donate electrons and the latter predicts the ability of the surface to receive electrons. Thus, we can readily *interpret* the physics in the model derived from the LASSO+ l_0 workflow because it is simple. However, the model still is not *comprehensible* in the most rigorous sense because we have not described how the model can be constructed from foundational physical principles. A deeper analysis of the 3D model with three descriptors shown in Table 1 suggests that it may be possible to arrive at such

comprehensive models. The 3D model captures subtle physics that are missed by the 1D model, which only described simple charge transfer. In particular, the 3D model includes a term that captures the formation of metal–metal bonds, which can form in certain cases, as shown by the charge-density difference plots in Figure 5. This term is

$$\left| \frac{IE_2^m - IE_4^s}{IE_2^m} \right| \times \left((\eta^m)^{\frac{1}{3}} - (\eta^s)^{\frac{1}{3}} \right)^2 \quad (1)$$

where IE is the ionization energy of the adsorbed metal (m) or cation metal in the surface (s) in the 2+ or 4+ oxidation state, and η is the electron density at the boundary of the metal's Wigner–Seitz cell. This descriptor can be reexpressed in a form that is closely related to a physical model proposed by Miedema et al. [57] to predict the cohesion energy between bulk metals when they form a bimetallic alloy. Miedema et al. [57] showed that the enthalpy of alloy formation for two metals (A and B) should be proportional to two parameters:

$$(\phi^A - \phi^B)^2 \quad (2)$$

and

$$\left((\eta^A)^{\frac{1}{3}} - (\eta^B)^{\frac{1}{3}} \right)^2 \quad (3)$$

where ϕ is the work function of the metals. Comparing Eq. (1) with Eqs. (2) and (3), we see that the LASSO+ l_0 workflow arrived at a similar prediction. Using a Pearson correlation metric (r), we find that the first term in Eq. (1) correlates strongly with the square of the differences of the ionization energies (i.e., $r = 0.98$). Thus, we could reexpress Eq. (1) as

$$(IE_2^m - IE_4^s)^2 \times \left((\eta^m)^{\frac{1}{3}} - (\eta^s)^{\frac{1}{3}} \right)^2 \quad (4)$$

Thus, the LASSO+ l_0 workflow derived an expression that is closely related to the Miedema model for computing the metal–metal cohesion energy. The work-function term in the Miedema expression describes charge transfer and is appropriate for predicting the

cohesion energy when an alloy is formed between two bulk metals. That term was replaced with ionization energies by the LASSO+ l_0 workflow, which is appropriate for describing charge transfer between single-metal atoms instead of bulk metals. This example shows how SR has the potential to derive *comprehensive* models relevant for catalytic materials with less than 100 training data points, albeit with help from the domain knowledge of the user.

Though SR has proved successful in several cases for constructing physical descriptors, a key drawback in the CS framework is the large number of candidate descriptors generated during the one-shot feature-engineering step. The GA-SR algorithm progressively builds descriptors by mimicking natural selection. Only the fittest descriptors are propagated forward and thus the size of the candidate-descriptor pool is managed. The one-shot CS framework enumerates all possible combinations of the user-defined operators, which quickly leads to an enormous descriptor space (e.g., with billions of candidates). Furthermore, the descriptors in that space are all highly correlated as a result of the recursive feature-engineering process, which creates challenges for the feature-selection step. Scheffler and coworkers proposed a hierarchical framework of SISO to address this challenge [58], wherein a first round of SISO is applied to obtain descriptors that are then fed into a successive round of SISO. This generates a hierarchy of increasing complexity by only propagating selected features. Our group has developed a similar strategy, called iterative Bayesian additive regression trees (iBART) [52,53], that also seeks to minimize the size of the candidate-descriptor space by interleaving feature-selection and feature-engineering stages. iBART implements Bayesian additive regression trees (BART) to identify nonlinearly correlated features from the primary feature space. The selected features are then engineered to populate the next generation of descriptors, which are then treated as the input for the next round of BART feature selection. This iterative approach significantly reduces the size of the feature space from $\sim 10^6$ to $\sim 10^3$ candidates. Thus, iBART can efficiently build complex descriptors while only requiring a fraction of the computational resources needed for the one-shot methods.

Finally, we comment on the limitations of SR models for tackling the complex nature of real-world heterogeneous catalysts. The systems we discussed here represent highly simplified models of the catalyst surface under reaction conditions. From these studies, we realize that SR can capture the main physics in the data with a handful of descriptors, but only for reasonably well-defined systems. We cannot expect SR to unravel all competing effects simultaneously, but we can expect it to provide ways to systematically improve the physical models we have in hand. This is exemplified by the

above study of metal–oxide interactions. The first descriptor identified by the SR algorithm captures metal–oxygen interactions that were already well understood; the second and third descriptors refine the model by capturing subtle effects arising from metal–metal interactions that previously were not considered important. These results show how SR can address complexity in catalytic systems. Of course, SR applications in catalysis are still in the developmental stage and many challenges remain in applying SR to describe the full complexity of real-world catalytic systems. Strong collaborations between statisticians, chemists, materials scientists, and engineers will be required to overcome these challenges.

Conclusions

The studies highlighted here demonstrate how SR can be a useful tool for finding physical insights in catalytic systems with ML. Nonetheless, the trade-off between model complexity and explainability is still a challenge. Although SR offers a promising path forward, SR-derived models are not inherently *comprehensible* because the resulting functions can still be too complex to interpret. SR provides analytical expressions for computing useful quantities, but it ultimately is the task of the scientist to interpret what those expressions mean. Indeed, it is just one's ability to apply domain knowledge that separates an interpretable model from a comprehensible model. From primary feature collection to extracting the underlying physics, domain knowledge is the key for constructing *interpretable* and *comprehensible* models. We have shown some examples wherein SR can lead to functional forms that we can recognize as known physical models in catalytic systems. These examples also show how SR provides signposts for improving physical models, which ultimately may lead to entirely new theories. Finally, we note that SR is ideal for studying catalytic systems when only small data sets are available for model training because it generates parsimonious models that are resistant to overfitting. For example, Weng et al. [36] showed that SR could identify an effective physical descriptor for predicting new OER catalysts using a training set of experimental data for just 18 perovskite compositions.

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Declaration of Competing Interest

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