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Multiscale Modeling for Emergent Behavior, Complexity, and Combinatorial Explosion

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Introduction

Multiscale modeling is rooted in early stages of scientific modeling. Constitutive equations, such as Fick's first law, which are routinely employed in engineering applications, describe macroscopic cause/action (gradient/flux) relations and constitute *ad hoc* coarse-grained forms of microscopic physics. Similarly, a rate constant is a coarse description, whereby details of the reaction coordinate, transition states, orbitals, etc., are left out. Implicit integration schemes have successfully been developed to deal with separation of time scales (stiffness) in solving ordinary differential equations, and adaptive mesh refinement strategies have been implemented to cope with separation in length scales of partial differential equations.

These examples and a multitude of others testify to the fact that (the often nonrigorous) coarse-graining and information passing between scales have been commonplace in engineering practice and teaching. It is clear that we have been exercising multiscale modeling since the beginning of our profession, but it may be less clear what is new in the modern era of multiscale modeling over the past 15 years or so. In modern multiscaling, one attempts to coarse-grain a molecular scale model in a mathematically rigorous way and/or couple models and phenomena across two or more scales (Vlachos, 2005). The latter approach necessitates coupling of mathematically different or so-called hybrid models, such as stochastic and deterministic or continuum and discrete. An example is the coupling of quantum mechanical density functional theory (DFT) calculations with a kinetic Monte Carlo (KMC) method or a molecular dynamics (MD) simulation, or the coupling of a KMC simulation with a macroscopic (process) computational fluids dynamic (CFD) simulation.

The emphasis of modern multiscale modeling has been mathematical—and algorithmic-centric; researchers have focused on developing and benchmarking methods to couple models across scales and accelerating simulation at each scale. Select major mathematical and computational milestones of this early work are summarized in Figure 1. As a result of this developmental focus, the engineering problems tackled have by-and-large been simple.

Moving from prototype problems to cutting-edge applications in biotechnology, nanotechnology and energy requires a conceptual shift in the modeling approach since these problems exhibit often emergent behavior, complexity, and combinatorial explosion in the number of models and parameters. Multiscale modeling that copes with these topics is in rather embryonic stages. In this article, we provide a perspective on the role that multiscale modeling can play in coping with these challenges. The illustrations of multiscale modeling will be drawn from two areas of applications. The first includes the fabrication of materials whose evolving structure/morphology exhibits emergent behavior due to self-organization, the control of which is challenging due to thermal fluctuations and nanoscopic dimensions. Also, the properties of such materials are emergent, making their prediction, e.g., activity of a catalyst, via intuition impossible. The second area of applications is heterogeneous catalysis, mainly for processing biomass to produce fuels and chemicals; the corresponding examples give rise to the topics of complexity, combinatorial explosion, and model-uncertainty and how they may be addressed within the context of multiscale modeling.

Emergent Material Structures with Emergent Properties

Emergent structures via self-organization

Self-assembly constitutes the backbone of *bottom-up fabrication* of nanomaterials, created via aggregation of individual building blocks (atoms, molecules, nanoparticles).

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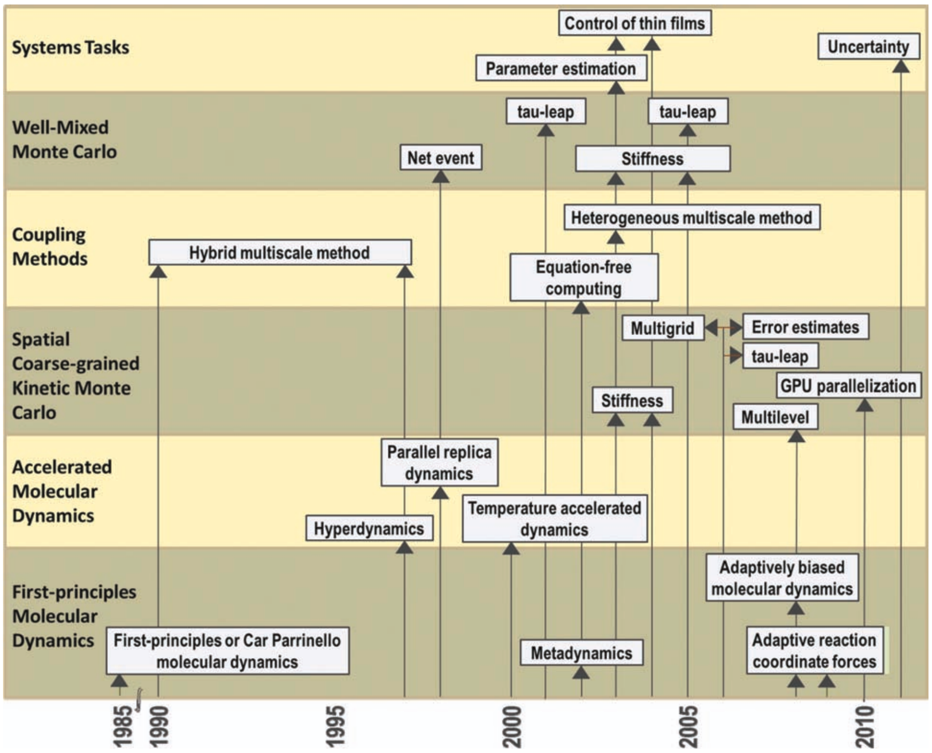


Figure 1. Select major milestones in multiscale modeling.

Methods entail the first-principles or Car Parrinello molecular dynamics (CPMD) (Car and Parrinello, 1985) and its accelerated versions, including the metadynamics (Laio and Parrinello, 2002), adaptively biased molecular dynamics and adaptive reaction coordinate forces (Babin et al., 2008; Barnett and Naidoo, 2009); the accelerated molecular dynamics (hyperdynamics, parallel replica dynamics, temperature accelerated dynamics (Sorensen and Voter, 2000; Voter, 1997; Voter, 1998); spatial coarse-grained kinetic Monte Carlo methods including stiffness (Chatterjee et al., 2004; Katsoulakis et al., 2003), tau-leap (Chatterjee and Vlachos, 2006), multigrid (Chatterjee and Vlachos, 2006), multilevel (Katsoulakis et al., 2008), error estimates (Chatterjee and Vlachos, 2006; Katsoulakis et al., 2006), GPU parallelization (Xu et al., 2010); accelerated well-mixed Monte Carlo simulation including stiffness (Chatterjee et al., 2005; Rao and Arkin, 2003; Rathinam et al., 2003; Salis and Kaznessis, 2005), net event (Vlachos, 1998), tau-leaping (Chatterjee et al., 2005; Gillespie, 2001); accelerated particle methods such as the tooth-gap method (Gear et al., 2003); coupling methods such as the equation free (Makeev et al., 2002), the heterogeneous multiscale method (Weinan et al., 2003), and the hybrid multiscale method (Vlachos, 1997; Vlachos et al., 1990); and system tasks including parameter estimation (Drews et al., 2003), control of thin films (Armaou et al., 2004; Lou and Christofides, 2003), and uncertainty quantification (Ulissi et al., 2011).

Hierarchical (with order over multiple length scales) *self-assembly* (e.g., from building blocks to nanoparticles to ordered arrays of nanoparticles; see Figure 2) is technologically important for inexpensive, large-scale manufacturing of nanostructures with desired size, shape, and lateral order. Such hierarchical nanostructured devices find applications ranging from solar cells, to microelectronics, to magnetic storage media, to composite membranes, to catalysis (e.g., zeolites). The technological significance of self-assembly has driven major research efforts toward the understanding of the fundamental mechanisms of self-aggregation (Alivisatos, 1996; Pohl and Heffelfinger, 1999; Seul and Andelman, 1995; Stradner et al., 2004).

While the underlying detailed physics in self-organization is system specific, a common theme in all applications (ranging from colloids to biology to materials) is that patterns form from the interplay of short attractive interactions and long repulsive interactions. The former (e.g., van der Waals interactions) bring matter together, whereas the latter (e.g., electrostatics, strain induced interactions) keep material apart to prevent continuous agglomeration of matter via Ostwald ripening. The formation of arrays of metal clusters and quantum dots on crystal surfaces of a different material, that is, in heteroepitaxy, with a narrow shape and size distribution (Brune, 1998; Dagaut et al., 1987; Masumoto and Takagahara, 2002), is such a prototypical example of self-assembly and is further discussed here.

In a typical *experimental protocol*, one deposits a certain amount (hereafter called loading) of material A on material B followed by annealing at a specific temperature for a certain time. Under certain conditions (e.g., sufficiently low temperatures), patterns form. The observables (size, shape, density, lateral organization, defects) of these patterns depend on a limited number of experimentally manipulated variables, such as temperature, loading, strain field, and material properties (Vasco, 2004). Experimentally, one typically varies one manipulated variable at a time (a parametric study) to optimize structures. The primary physical mechanism via which self-organization takes place is surface diffusion.

Design and control of emergent structures: challenges and opportunities

The very issue of the spontaneous character of self-assembly that allows scale-up of devices with features at the nanometer scale is also the core source of difficulties on how to

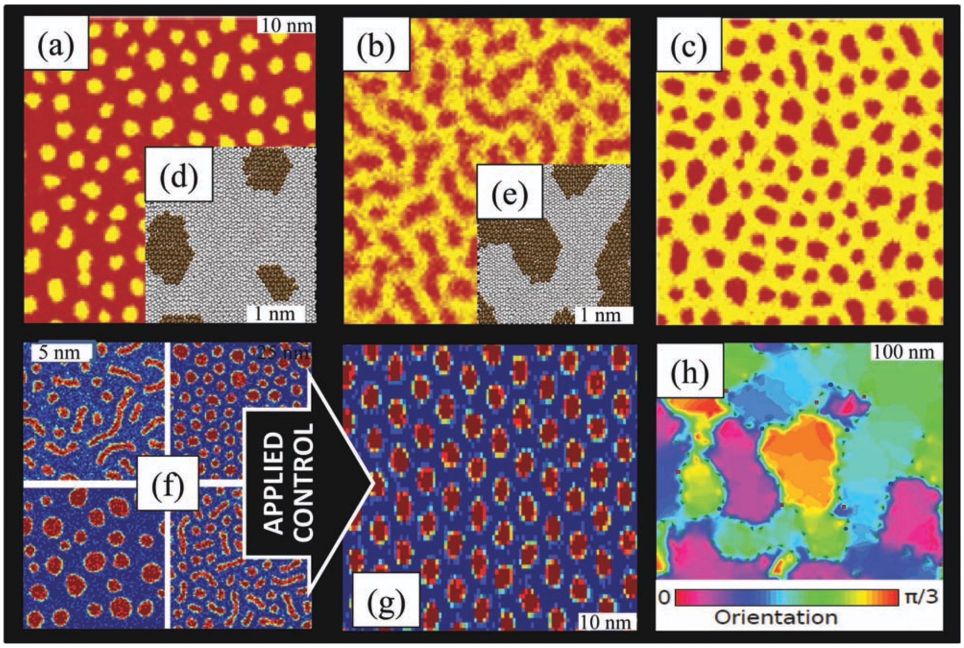


Figure 2. Emergent structures in self-organization during heteroepitaxial growth of materials.

Figure 2a–c: Coarse-grained kinetic Monte Carlo simulation patterns as the (submonolayer) coverage of the over-layer metal increases (low loading: defected hexagonal structure; medium loading: labyrinths; high loading: inverted nanodots) (Chatterjee and Vlachos, 2007). (d) and (e) molecular dynamics snapshots for approximately the same loading, as in (a)–(c), for a Ni overlayer on top of a Pt crystal (Wang et al., 2010), (f) snapshots of coarse-grained Monte Carlo simulations for slightly different operating conditions illustrating the sensitivity of patterns to manipulated variables, (g) structure obtained using optimal control with a response surface-reduced model of coarse-grained Monte Carlo simulations indicating sufficient hexagonal ordering (Chatterjee, 2007), and (h) postprocessing results of mesoscopic simulations illustrating defects at device length scales (much larger than those of (a)–(c)) through local hexagonal domain orientation: +/− disclinations (red squares and blue circles, respectively), dislocations (green arrows), and anisometric pattern features (red circles); from (Abukhdeir and Vlachos, 2011). Such defect accounting is used to formulate an objective function for optimal control theory aiming at minimizing defects. The length-scale bars in panels (a), (d), and (h) indicate the difference in scales achieved using different computational methods for the same problem.

design the desired structure and control the fabrication of such systems over a hierarchy of length and time scales (Masumoto and Takagahara, 2002). As a result, design and control of these systems still eludes the researchers' full grasp. Some of the challenges entail that these systems have truly emergent complex behavior, whereby one cannot predict *a priori* the collective behavior of the system from its building blocks. Under certain conditions, small variations in these manipulated variables result in profound changes of patterns (Figure 2f). Furthermore, the state variables are of extremely high dimension; these are truly "distributed parameter systems" and exhibit intrinsic stochastic fluctuations. The systems exhibit *poor controllability*: nanoscale features over several orders of magnitude are to be controlled using a mere handful of manipulated variables (e.g., temperature, loading, strain field) available only at the macroscale. Actual measurements of features to be controlled are usually impossible to obtain online; probe microscopy images (AFM, STM) are obtained only after processing is complete, leading to *poor observability*.

The aforementioned points paint the challenges for both control and model development. In the chemical engineering literature, stochastic model-based control of the roughness of thin films has been introduced (Lou and Christofides, 2003; Varshney and Armaou, 2008). This control problem amounts to controlling a spatially average metric (roughness). Pattern formation, discussed herein, is naturally a much harder control problem.

What about our ability to develop first-principles-based multiscale simulations for self-assembly of heteroepitaxial growth with the ultimate goal of model predictive control? Modeling these systems for control purposes is nontrivial for two reasons: Interactions and dynamics are manifested over broad ranges of spatial and temporal scales, and along with stochastic thermal fluctuations they challenge any first-principles-based computations, such as molecular dynamics (MD) (Chatterjee and Vlachos, 2007). As a result, reduced models, which are derived from fundamental principles for design and control, have also been lacking. A general strategy for model-based control of self-assembly has not been proven yet.

Prior modeling efforts have attempted to capture the experimentally observed rich variety of patterns (Plass et al., 2001). One such class of models entails equilibrium-free energy-based models (Daruka et al., 1999; Meixner et al., 2001; Ng and Vanderbilt, 1995) that predict the most energetically stable pattern at zero Kelvin. Given the importance of entropy at higher temperatures and the lack of dynamics, these models are unsuitable for control. A second class entails phenomenological dynamic models, such as phase field, Cahn-Hilliard, and Allen-Cahn models. These have been extensively employed to predict phase diagrams in alloys and polymer matrices (Cahn and Hilliard, 1958; Glotzer et al., 1995; Guyer and Voorhees, 1995; Leonard and Desai, 1998). However, they lack thermal fluctuations and microscopic-based free-energy functionals, rendering the kinetic pathway traced by such models questionable. More recently, molecular scale models, such as the lattice kinetic Monte Carlo (KMC) simulation, have gained attention. KMC can incorporate the correct microscopic physics, entropic effects, and thermal fluctuations, which are essential for correctly modeling nanoparticle nucleation and growth (Katsoulakis et al., 2003; Vlachos, 2005). Despite recent advances in developing efficient KMC algorithms (see (Chatterjee and Vlachos, 2007) for a review; Figure 1), generation of phase diagrams via KMC is still challenging due to large separation of length scales (from <1 nm for single atoms, to 1–10 nm for nanoparticles and long-range potentials, to 100–10,000 nm for arrays of nanoparticles collective emergent structures), and time scales (from 1 ps to 1 min). The computational costs are truly prohibitive due to long-range interactions and slow organization over long-time horizons. For example, a microscopic KMC simulation for the patterns shown in Figure 2a–c can take up to 6 months on a single processor.

With the goal of developing a unifying modeling framework for self-assembly processes on surfaces, in the last few years, the author and his collaborators have been developing a bottom-up hierarchy of coarse-grained models. This hierarchy starts from KMC models and includes the coarse-grained kintic Monte Carlo (CG-KMC) method and continuum mesoscopic (partial integro-differential) equations (Chatterjee et al., 2004; Chatterjee and Vlachos, 2006; Chatterjee et al., 2004; Katsoulakis et al., 2003; Vlachos and Katsoulakis, 2000). The latter are reminiscent of the well-known Cahn-Hilliard and Allen-Cahn models, but are directly linked with the microscopic KMC processes. They are computationally inexpensive (Abukhdeir et al., 2011), but do not account for stochastic thermal fluctuations. In contrast, the CG-KMC method retains the correct fluctuations. However, it is still computationally intensive to use for systems' tasks, e.g., to generate a phase diagram or to carry out control (e.g., simulations that generate structures like those in Figure 2a–c take about 1 day to perform on a single processor).

In order to efficiently study pattern formation, the author and his collaborators proposed a systematic top-down modeling approach, using the hierarchy of coarse-grained models (e.g., mesoscopic equations and CG-KMC) symbiotically (Chatterjee and Vlachos, 2007). A phase diagram of nanopatterns is generated via linear and nonlinear analysis of mesoscopic equations. CG-KMC simulations are subsequently performed at selected points of the phase diagram to provide distributions of nanoparticle size, shape, interparticle spacings, etc. Results from this hierarchical simulation framework are in excellent qualitative agreement with experimental results (e.g., on Pb/Cu(111) (Plass et al., 2001)). Patterns vary from hexagonal at low coverages of Pb, to labyrinths at intermediate coverages, to inverted nanodots (continuous layer with nanosized holes) at high coverages, as shown in Figure 2a–c.

As a first attempt toward controlling patterns, they have parameterized the output of the stochastic CG-KMC model with an empirical response surface (Chatterjee, 2007). This reduced, empirical, model was subsequently used for optimal control, whereby the strain and temperature were varied as a function of time to minimize a certain objective function. The objective function was based on simple structural characteristics (particle size, local hexagonal order, distance between particles, etc.). Typical results are shown in Figure 2g.

These initial results indicate that some degree of controllability on nanopatterns formation is indeed feasible. However, more work is needed to overcome the aforementioned modeling and control challenges. A detailed characterization of defects over multiple length scales (e.g., point defects, disclinations, and dislocations) has recently been carried out (Figure 2h) in order to develop objective functions that are applicable to device length scales (Abukhdeir and Vlachos, 2011), i.e., at scales much larger than those shown in Figure 2g. Interestingly, the scaling laws for formation of these defects are reminiscent of those in block copolymer literature. Developing reduced models and understanding how controllable these systems are form an essential future research direction for creation of best manufacturing strategies.

Chemistry on a dynamically varying environment

While the coarse-grained Monte Carlo method captures experimentally accessible spatial and temporal time scales, it has several shortcomings. First, it is based on an on-lattice approximation, and second, it lacks the spatial resolution of an atomistic simulation. Molecular dynamics and its accelerated forms (Figure 1) can provide pathways from ns up to ms times, respectively. For example, identification of diffusion pathways is important since, for instance, in bimetallic systems, aside from diffusion of one metal on top of the other, mixing of metals is also possible. In a recent study on surface bimetallics (Ni over-layer on a Pt film), we employed a broad toolset (simulated annealing, molecular dynamics and accelerated molecular dynamics simulations, classic nudge elastic band (NEB) calculations, and experiments) to address the disparity of time scales (Wang et al., 2010).

It was found that at lower temperatures, the system is metastable (kinetically trapped) and the overlayer (Ni) exhibits fast dynamics (in the order of ns) under typical reaction conditions. Dynamic restructuring of the Ni overlayer at these short time scales cannot easily be observed experimentally. Scanning probe methods at low temperatures may possibly capture this dynamic behavior. As a result of this fast dynamics, the chemistry occurs in a dynamically fluctuating environment rather than a static one that is typically cartooned in textbooks and research publications. Figure 3 shows the time-averaged distribution of the first shell coordination numbers of Ni and Pt to illustrate that there is no static catalyst structure. At higher temperatures, mixing occurs, whereby Ni diffuses into the bulk of Pt, enriching every other layer (Wang et al., 2010).

Aside from the dynamics of surface bimetallics discussed here, additional dynamic phenomena, such as reconstruction and oscillations of nanoparticle shape upon heating, most probably happen. Overall, our understanding of catalyst dynamics is in embryonic stages. Our ability to predict the catalyst dynamics and its effect on kinetics is severely lacking. Future work should include the development of methods to

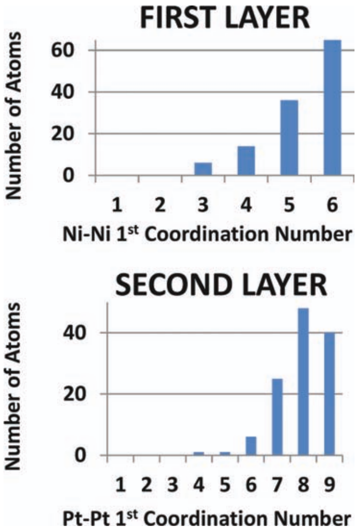


Figure 3. Statistical properties of Ni/Pt heterostructures arising from the dynamics of the catalyst.

Time averaged molecular dynamics-based coordination number distribution functions of Ni in the first layer and Pt in the second layer from calculation shown in (Figure 2d) (Wang et al., 2010).

explore the effect of adsorbates on the catalyst dynamics, the evolution of nanoparticle dynamics on a support, and the impact of catalyst dynamics on kinetics and catalyst performance.

Emergent properties of surface bimetallic systems

The aforementioned discussion has focused on patterns and their dynamics. Next we turn to the properties of such heteroepitaxial systems and specifically to adsorption. While the properties of bulk alloys can often be approximated as linear interpolations of those of single parent metals, this is not true for surface bimetallics. An example is shown in Figure 4, which compares the computed binding energies of nitrogen on Ni, Pt, and two Ni/Pt architectures. Interestingly, the binding energies of atoms on the surface Ni-Pt-Pt and subsurface Pt-Ni-Pt (in the X-Y-Z notation, X stands for the top layer (surface), Y for the second layer (subsurface), and Z for the bulk metal) architectures are not between those of the parent metals (single crystal of Ni or Pt). Such emergent properties result from the hybridization of atomic orbitals (lattice mismatch and ligand effects) of the two metals and can be rationalized as a shift of the d-band center of the metals with respect to the Fermi level (Chen et al., 2008).

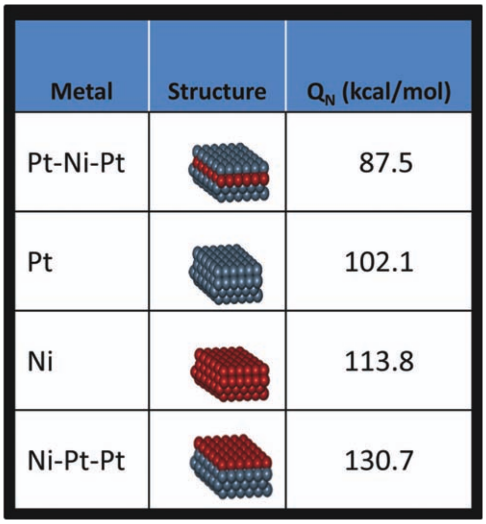
Since binding energies correlate strongly with kinetics, surface alloying has a profound effect on activity and selectivity (Chen et al., 2008). The former correlates linearly with the distance of the d-band center from the Fermi level. No such correlations exist for selectivity. Thus, while this emergent adsorption behavior renders prediction of surface bimetallics apparently hard, it paves the way to discovering new materials whose properties are superior to those of single metals by selecting a suitable binary and by controlling the molecular architecture of the material. This topic is elaborated in the next section where a methodology for multiscale model-based prediction of such materials with desirable catalytic properties is presented.

These surface bimetallics are not difficult to make on single crystals. However, synthesis of the corresponding core–shell nanoparticles on supports is a major undertaking. Furthermore, the stability of these nanoparticles against sintering, intraparticle mixing, and in response to their environment (e.g., upon exposure to different adsorbates) remains an open problem for future research. Aside from selecting a specific binary alloy (e.g., Ni and Pt), the effect of loading is poorly understood— the monolayer cartoon of one metal on another (Figure 4) is too simplistic as molecular dynamics simulations show (see Figure 3). One can envision a bifunctional catalyst where part of the chemistry happens on bimetallic clusters (e.g., Ni on Pt), and the rest on exposed Pt patches. Consequently, the loading of the over-layer provides another knob that can be optimized for fabricating the next generation catalysts but nearly no work has exploited this opportunity.

Complexity, Combinatorial Explosion, and Uncertainty in Catalytic Kinetics

Recent advances in modeling of catalytic reactions and reactors

Catalysis is the pillar of the chemical and refinery industry. The complexity of heterogeneous catalytic processes has eluded researchers and demanded significant empiricism by practicing engineers to run, optimize, and control chemical plants. Given the profound industrial success over the past century and the current slow manufacturing growth in the United States, a natural question is what multiscale modeling can provide to this rather well established field. Aside from



Metal	Structure	Q_N (kcal/mol)
Pt-Ni-Pt		87.5
Pt		102.1
Ni		113.8
Ni-Pt-Pt		130.7

Figure 4. Binding energy of nitrogen atoms, Q_N, on various idealized bimetallic surfaces.

Depicted are single metals of Pt and Ni, surface Ni-Pt-Pt and subsurface Pt-Ni-Pt bimetallics. Binding energies obtained via density functional theory (Hansgen et al., 2010).

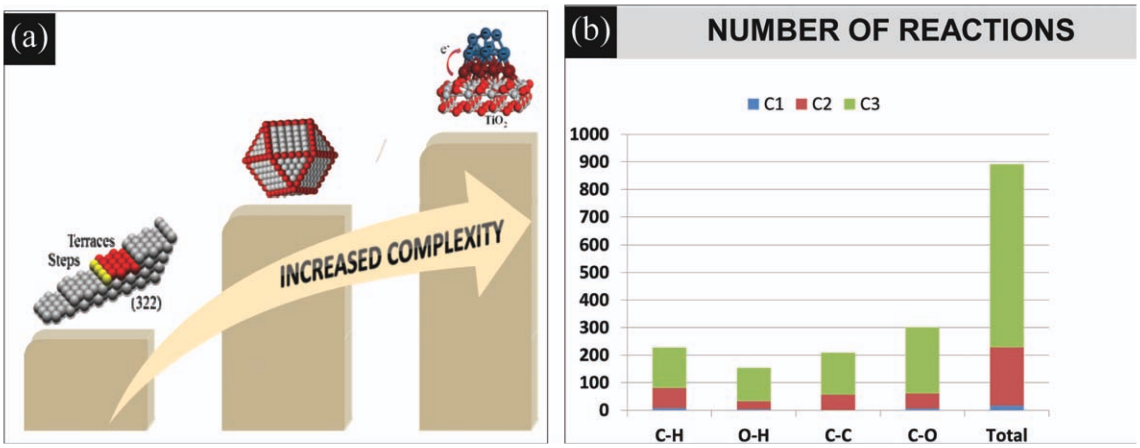


Figure 5. Complexity arising from materials gap and number of reactions.

(a) Schematic illustrating the materials gap from single crystal to unsupported metal nanoparticles to supported metal nanoparticles, (b) number of chemical reactions for catalytic pyrolysis of different types of reactions in one carbon oxygenates (methanol (C1)), two carbon polyols (ethylene glycol (C2)), and three carbon polyols (glycerol (C3)). The stacked bar shows all reactions needed for glycerol modeling for each type of reaction.

providing fundamental insights into a process, multiscale modeling can supply thermophysical data and kinetics at an accelerated rate and reduced cost and can replace experimentation, when the latter is difficult or safety is of concern. Over the past 15 years, CFD simulations have become a rather routine tool at the macroscopic (process unit) scale for design and optimization (especially for laminar flow systems). The design of microsystems for portable and distributed energy generation is one successful demonstration of CFD in emerging chemical engineering areas (Vlachos and Caratzoulas, 2010). The area of renewables and alternative fuels, driven by global warming and/or energy independence, provides opportunities for design in new manufacturing facilities (Vlachos and Caratzoulas, 2010). Despite significant progress, turbulent flows, multiphase transport phenomena, and incorporation of detailed kinetic models in CFD simulations still challenge practitioners and academics alike. Yet, the macroscopic-scale process-modeling is considered a fairly mature field.

Materials needed for catalytic processes have been discovered via trial-and-error in single reactors or recently in high-throughput systems, but overall progress has been slow. Multiscale modeling can have profound impact on discovery of novel materials for different reactions. In other words, multiscale modeling could assist process design but more importantly enable product design (Vlachos et al., 2006). This requires a fundamental understanding of the underlying chemistry.

In order to understand reactions on metal catalysts and isolate chemistry from support and reactor effects (transport, fluid flow), surface science single crystal, ultrahigh vacuum research has flourished in the academic community from 1970s to 1990s. This focus has led to a significant gap between fundamental experiments on model surfaces and applied, catalytic reaction engineering (Figure 5a) and raised serious criticisms for the relevance and impact of surface science, leading to significant shrinking of this subfield.

In the mid-90s, quantum mechanical simulations and specifically density functional theory (DFT) started emerging as an indispensable research tool in heterogeneous metal-based catalysis. The advances in accuracy and computational power have propelled profound scientific progress made via using DFT. The location of the d-band center with respect to the Fermi level has been proven to be an excellent descriptor of catalyst activity (Norskov et al., 2002). Rate constants have been computed, spectroscopic data have been explained, new pathways have been discovered, mechanisms have been built, and detailed surface reaction (microkinetic) model predictions have been compared to experimental data (Salciccioli et al., 2011; van Santen and Neurock, 1995).

More recently, the concept of the volcano curve has been explored computationally to identify catalysts with superior activity than single metals or inexpensive metal alloys with comparable activity as that of noble metal catalysts (Jacobsen et al., 2001). Based on the Sabatier principle, the catalyst activity is highest when the binding energy of reactants and products is moderate; high-binding energies lead to blocking and poisoning of catalyst sites; low-binding energies lead to fast desorption and insufficient residence time of reactants and, thus, to low conversion. Catalyst activity (reaction rate) is typically graphed as a function of the binding energy of the dominant adsorbate. One can easily compute via DFT the binding energy of an adsorbate on various catalysts and map the reaction rate—through a Langmuir-Hinshelwood rate expression—as a function of this binding energy (a few equilibrium constants may also be needed in evaluating the reaction rate). One can then estimate via linear interpolation the composition of a mixed alloy on which the binding energy is close to the maximum of the volcano curve from those of two parent metals. A few such successful results have led to excitement about the prospect of computer-aided catalyst design (Jacobsen et al., 2001). Obviously, emergent bimetallic catalysts discussed earlier (Figure 4) cannot be predicted using interpolation.

Challenges in first-principles' catalytic reaction modeling

Despite the profound impact computational methods have had on catalysis and reaction engineering over the past decade, there are still major conceptual challenges awaiting solution. Biomass processing is used as an example to outline some of these challenges.

The first overarching challenge entails parameterization of rate constants. The majority of computational work has focused on simple molecules and simple reactions on metal slabs (chunks of metals in contact with a vapor). Examples of reactions include the CO oxidation, the NH_3 synthesis, the water-gas shift, and the CH_4 pyrolysis and oxidation on noble metals. There is obviously a need to go beyond such simple molecules and reactions, especially for biomass processing, but computational cost increases drastically with molecular size beyond current computational resources. For example, in catalytic pyrolysis of oxygenated molecules (Figure 5b), the number of reactions scales from tens in methanol to a few hundred in ethylene glycol (the smallest polyol) to nearly one thousand in glycerol (the three carbon byproduct of biodiesel). This number of reactions is even larger when coreactants are considered, as happens in steam reforming or oxidation. The sheer size of biomass derivatives (e.g., sugars) and the numerous pathways that can occur, especially when bonds break unselectively, require significant computational resources to estimate the rate constants for each molecule. In simple terms, there are too many parameters to compute quantum mechanically for a single compound. Given the large number of components of bio-oil, building a kinetic model for each single compound using first-principles simulations is even a bigger undertaking. These facts point to an explosion in both the rate parameters and the number of mechanisms. Further complication arises from the fact that the biomass feedstock varies with season and type of biomass, and the bio-oil composition depends significantly on pyrolysis conditions. It goes without comment that the development of a first-principles microkinetic model on different catalysts requires repeating all the work on each metal. Clearly first-principles-based microkinetic models for biomass processing are beyond our current supercomputing capabilities.

A rather overlooked complication in large molecules, such as sugars and furans, is that these molecules contain many heteroatoms and/or rings and can adsorb on a surface in multiple, nearly isoenergetic configurations. Furthermore, the most stable structure can be a function of coverage of an adsorbate and dependent on the catalyst. The ramification of this multiconfigurational adsorption state is that one reaction mechanism is required for every configuration of each intermediate. Isomerization reactions, which convert one configuration to another, connect these mechanisms and lead to an explosion in adsorbate and mechanism accounting, which has not been dealt with before in catalytic kinetics. Simply too much computing is needed to estimate all these rate parameters. This floppiness of structures is even more eminent in solution chemistry; statistical mechanics, while computationally cumbersome, is necessary to properly weigh all configurations and their effect on each reaction rate constant.

A single set of reaction rate parameters of an elementary chemical reaction in the gas-phase describes each reaction event (a two-body collision). In contrast, the parameters of a surface reaction depend strongly on the presence of coadsorbates, their nature, and their exact location. In other words, a surface reaction event is a many-body problem and the parameterization of the reaction rate constant as function of all adsorbate coverage's and locations leads to yet another combinatorial explosion (Salciccioli et al., 2011). These (commonly known as) lateral interactions are often neglected or at best treated approximately by expressing the activation energy in terms of the overall coverage of a single adsorbate (a mean field approximation). Computing all pair interactions in large multicomponent systems is, even within the mean field approximation, computationally prohibitive. Complete omission of coverage effects is a severe oversimplification leading to poor model predictions. Proper parameterization through a Hamiltonian and cluster expansion is feasible (Salciccioli et al., 2011) but is daunting for complex systems.

Solvent dynamics is too important to suppress especially in acid catalyzed chemistry, such as sugar isomerization, dehydration, esterification, and etherification. Treating reaction events with statistical mechanics necessitates the use of molecular dynamics (MD) simulation coupled with importance sampling to handle barriers of chemical reactions (Figure 1). Since most force fields are incapable of treating chemical bond breaking and making, a quantum mechanical treatment of the bonds that undergo changes is necessary. Hybrid quantum mechanics/molecular mechanics (QM/MM) MD simulation for the active region and the distant region of nonreactions, respectively, strikes a balance between accuracy and computational cost (Caratzoulas and Vlachos, 2011). An additional complication is that biomass reactions often involve concerted events leading to multidimensional surfaces rather than the single reaction coordinate picture of textbooks.

At the mesoscale, reaction rates are computed using first-principles input. These rates are finally incorporated in a pellet and/or reactor model (macroscale) to predict catalyst and reactor performance, such as conversion, selectivities, most abundant surface species, rate-determining step, etc. DFT-based rate constants are typically employed in a mean field model to compute reaction rates. Mean field models assume spatial homogeneity of catalyst and adsorbed species at the mesoscale, i.e., over a length scale that is small compared to the pellet or the reactor scale. As an alternative, kinetic Monte Carlo (KMC) simulations can account for catalyst and adsorbate inhomogeneity and their effect on reaction rates. A few such first-principles KMC simulations have been published but have not been widespread yet due to their computational cost, difficulty in analysis of the results, and lack of interfaces of KMC codes with quantum mechanical and macroscopic scale codes (Salciccioli et al., 2011).

Kinetic models are parameterized using DFT input on a single crystal, usually the (111) crystallographic plane. In reality, well-faceted nanoparticles (>2-3 nm) exhibit multiple crystallographic planes, all of which contribute in a nonlinear way to the overall activity. In addition, low-coordination sites, such as edges and corners (Figure 5a), are often more active than those of terraces. The effect of support on geometry, stability, and electronic state of nanoparticles is often not considered. In essence, models attempt to interpret experimental data of supported catalysts even though they capture only electronic effects of single crystals (Figure 5a). Finally, particle size and shape distributions, including small unfaceted clusters and catalyst dynamics can have a strong effect on kinetics. Currently, our understanding of all these

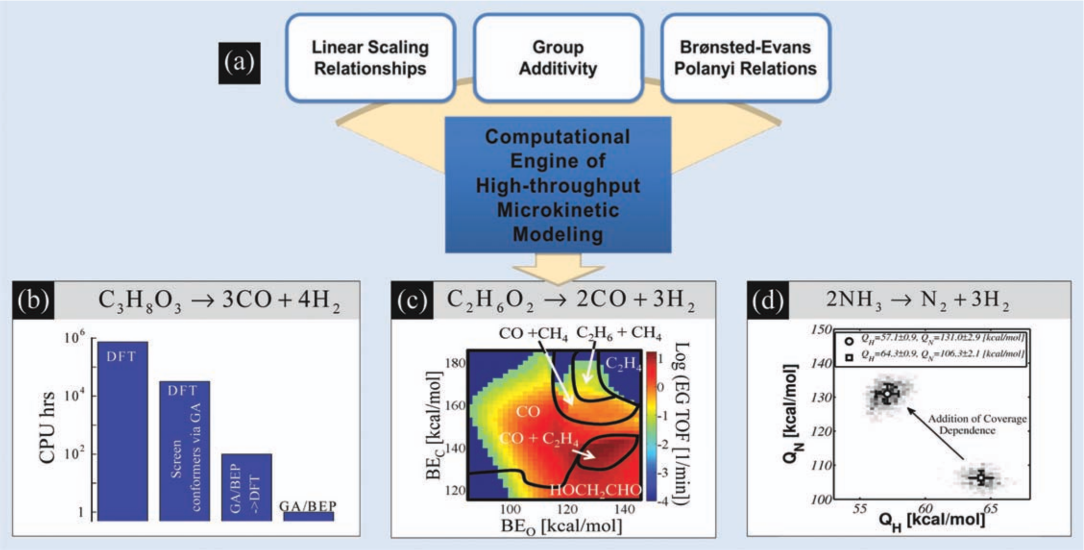


Figure 6. Hierarchical multiscale kinetic modeling.

(a) First-principles-based estimation methods for microkinetic modeling engine, (b) computational time in building the glycerol catalytic pyrolysis mechanism using DFT for all intermediates and reactions, or DFT for thermodynamically screened— via group additivity (GA)— intermediates and reactions, or DFT for thermodynamically screened, important intermediates and reactions (via combined GA and BEPs), or just first-principles-based semiempirical (GA and BEPs) methods. Four-orders of magnitude reduction in computational cost while maintaining DFT accuracy in important parts of the mechanism is achieved (Chen et al., 2011), (c) activity map (in color) with superimposed carbon selectivity for ethylene glycol thermal decomposition (Salciccioli and Vlachos, 2011), and (d) uncertainty analysis in activity map of ammonia decomposition with respect to an order of magnitude uncertainty in pre-exponential factors along with the effect of N-N lateral interactions (Ulissi et al., 2011). The latter shift the optimal catalyst properties from those of Ni and Pt and those of a Ni overlayer on Pt (Ni-Pt-Pt); Figure 4. Experiments indicate that the Ni-Pt-Pt surface bimetallic is superior than either of the single metals, in agreement with the model that accounts for interactions shown as the top left distribution (Hansgen et al., 2010).

structure-related phenomena is poor. Taking all these together, there is still a clear disparity in connecting single crystal DFT calculation data to the reactor scale. This disparity in length scales is reminiscent of the well-known materials gap between surface science experiments and supported catalysts. Future research should be devoted to closing this gap.

While Sabatier's principle describes catalyst activity with the binding energy of the dominant surface atom as a descriptor, similar descriptors about the harder problem of selectivity do not exist. In addition, models published on computer-aided catalyst design often employ a Langmuir-Hinshelwood rate expression derived with *a priori* assumptions about a rate-determining step and a single dominant surface species. Such assumptions break down over a wide range of operating conditions and/or binding energies. A full microkinetic model is necessary to overcome these hurdles and address the activity and selectivity topics simultaneously.

First-principles semiempirical estimation methods

Despite having a huge number of parameters in large kinetic models, these parameters are not actually independent. In essence, there is a low-dimensional manifold behavior in model parameterization; a few parameters are independent and the rest are slaved to those independent ones. The introduction of the hierarchical multiscale modeling framework (Figure 1) is one approach that leverages correlations between variables to systematically cope with the parameterization challenge (Chen et al., 2011; Mhadeshwar and Vlachos, 2005).

The first step in developing a detailed surface reaction model entails estimation of the thermochemistry, i.e., of the adsorbed species on a surface, their binding configurations, their binding energies, and how these change as a function of the coverage of the dominant surface species. To cope with the large number of species in bio-oil and the variability in molecular function in them (e.g., accounting for unsaturated carbon-carbon bonds, hydroxyl, carbonyl, carboxyl, and ether groups), we have developed a group additivity scheme. This scheme extends the original ideas of Benson for estimating thermochemistry in the gas-phase (Benson, 1976) to species on surfaces. It employs graph theory for identification of distinct groups and assigns thermophysical contributions to each group. It corrects gas-phase thermophysical properties for the difference in degrees of freedom resulting from adsorption and surface-related effects, such as strain of rings formed between a molecule with metal atoms, interactions of heteroatoms near the surface with the metal atoms, and inter- and intra-hydrogen bonds that are commonplace in biomass species (Salciccioli et al., 2011). The thermophysical contributions are obtained from a simple regression of a library of DFT data of representative, small molecular weight compounds. The end result is an automated code that runs in "no time" to estimate the thermochemistry of biomass derivatives (Figure 6a).

Due to the d-band center model, the energies of transition states scale linearly with either the energies of the reactants or products (van Santen and Neurock, 2010). In an alternative formalism, the activation barriers are correlated linearly with the heats of reactions. These linear free-energy or Brønsted-Evans-Polanyi (BEP) relations correlate in a simple way the barriers of surface reactions to thermochemistry (Figure 6a). The latter can be computed using the group additivity method and can account for lateral interactions, at least in a mean field sense. While BEPs have long been postulated for heterogeneous catalysis, DFT has provided a theoretical rationale for their existence and the possibility of defining suitable homologous series to increase model accuracy (van Santen and Neurock, 2010).

The introduction of linear scaling relations by Norskov and coworkers relates the binding energies of simple hydrogenated heteroatoms (OHx, CHx, NHx) with the binding energies of the corresponding heteroatoms (O, C, N) across metals of the periodic table. These simple relations enable one to estimate the binding energy of a species on any metal from those on another (Abild-Pedersen et al., 2007). The integration of linear scaling relations with the group additivity and the BEPs provides a lower accuracy (higher uncertainty) estimation method of the *hierarchical multiscale framework* (Figure 6a); other methods, such as bond order conservation, can also be used (Mhadeshwar and Vlachos, 2005). DFT provides the higher end in this hierarchy.

Materials' screening via high-throughput hierarchical multiscale computing

The aforementioned hierarchy can be exploited in different ways. Figure 6b provides one example of estimating rate constants for glycerol catalytic pyrolysis. Group additivity can be used to screen adsorbates that are thermodynamically unstable, and BEPs can then be used to eliminate reactions whose barriers are too large compared to competitive pathways. By combining the two tools, the remaining rather small set of adsorbates and reactions can be refined using DFT. In this approach, the estimation methods are used simply for screening and DFT for refinement of the key parameters. The end result is construction of a microkinetic model whose key parameters are obtained via first principles but at four-orders of magnitude less computational cost. An alternative approach employs the semiempirical methods only. This approach requires no additional computational cost upon developing the group additivity scheme and the BEPs (Figure 6a), but comes at the expense of larger uncertainty.

The combination of semiempirical estimation methods provides a powerful computational engine for calculating reaction rate constants of elementary reactions across the periodic table and, thus, for performing high-throughput computing. An example of using high-throughput computing to predict catalyst activity *and* selectivities maps to various products for catalytic pyrolysis of ethylene glycol is shown in Figure 6c. The model predicts pairs of (C and O) binding energies of materials resulting in high activity (deep red), and selectivity either to syngas, aldehyde, or hydrocarbons. Catalyst poisoning is demarcated with deep blue at high-binding energies at the top left, bottom right (not shown at this scale), and top right corners.

By creating a DFT database of binding energies of common elements (C, O, H, N, P, S) making up chemicals and fuels on multiple bimetallic architectures (e.g., surface and subsurface, Figure 4), one can readily screen compositions (e.g., Ni and Pt, Co and Fe, etc.) and architectures for each chemical reaction that are potentially suitable catalysts for high activity and/or selectivity based on the performance maps. We have recently reported microkinetic models that can do exactly this. Taking the ammonia decomposition as a prototype reaction, we predicted Ni-Pt-Pt as an excellent catalyst for hydrogen production (see Figure 2 and Figure 6d). The predictions were confirmed experimentally under ultrahigh vacuum conditions (Hansgen et al., 2010). The computational framework appears to be fairly robust in capturing electronic effects that dominate catalytic performance (Hansgen et al., 2011). An extension from activity to selectivity maps is depicted for ethylene glycol in Figure 6c (Salciccioli and Vlachos, 2011). These performance maps have been validated experimentally for some catalysts. While this is exciting progress, the catalyst stability and cost should also be accounted for in developing new catalysts.

Uncertainty in multiscale modeling

It is clear that first-principles reaction mechanisms can be built for small molecules and simple chemistries, but even then, there are various types of errors in the DFT estimates arising from convergence, functional, etc. More critical uncertainties arise from potentially missing reaction pathways and the approximate treatment of the catalyst structure (multiple facets, support effects; see Figure 5a), and adsorbate distribution (e.g., mean field vs. kinetic Monte Carlo) at the mesoscale. For larger molecules and reaction mechanisms where semiempirical methods alone are being employed, the error in the kinetic parameters is even larger than that of DFT. A more complete list of uncertainty factors is given in (Salciccioli et al., 2011).

Given model uncertainty, it is, therefore, important to assess the effect of uncertainty of the estimation methods at microscopic scale (parameters) and mesoscale (reaction rate, catalyst structure) on macroscopic reactor performance and prediction of new catalysts. Figure 6d shows an example of the effect of uncertainty in pre-exponentials (entropic terms), and lateral interactions in the ammonia decomposition chemistry on the optimal catalyst properties (Ulissi et al., 2011). Interestingly, uncertainty in most parameters results in a rather narrow distribution of optimal properties and plays no role in materials selection. However, the large lateral interactions between adsorbates on the catalyst surface strongly shift the optimal properties of most active catalysts. In this example, lack of interactions points to the wrong catalyst (Ni or Pt) instead of the bimetallic catalyst (Ni-Pt-Pt). This is the first-of-its-kind uncertainty analysis in microkinetic models. Obviously, much more work is needed to develop the methods and the understanding of the impact of uncertainty on model prediction and how to hierarchically refine parameters and physics to minimize it.

Data, data, and more data

Simulations generate a large body of data, but little of this is needed in practice or is passed in a model at a larger scale. For instance, in a DFT calculation, data on energetics, bond angles, bond lengths, vibrational spectra, etc., is generated, but only a binding energy or a reaction barrier is typically being passed to a kinetic model at the mesoscale. As another example, the reaction rate, which is an input into a larger scale CFD code, is just a spatial (mesoscopic) average over a KMC output distribution of microscopic rates. In both examples, significant data compression occurs when passing information from a finer to a coarser scale model. Similar compression applies in computing the self-diffusivity or adsorption isotherms using a molecular dynamics or a grand canonical Monte Carlo simulation, respectively. At the process scale, CFD generates detailed species, temperature, and fluid flow patterns, but a simple reactor model/output is needed in ASPEN for flow sheet calculations and optimization. The emerging theme from these examples is that data compression and model reduction are critical elements of multiscale modeling (Vlachos, 2005), and while various such techniques exist, methods for multiscale modeling and systematic data compression and a model reduction toolbox that can be employed by the scientific community are still needed.

Throughout this article, structures of bimetallics, libraries of binding energies, thermochemistry data, the output of semiempirical methods (linear scaling and free-energy relations), reaction mechanisms, reaction rate constants, etc., have been discussed. It is clear that organizing this information in a systematic manner for archival, search, and sharing purposes will be essential to avoid duplicating efforts and wasting resources. In this context, development of *chemin-formatics* is important as we move toward an extremely data rich era. An example is the use of bioinformatics tools, such as clustering, to organize the output of high-throughput microkinetic modeling for multiscale-based design of experiments (Prasad et al., 2010).

Outlook

Moving from the era of method-focused development to application-driven algorithms and simulations provides a robust, forward thinking toward a new generation of multiscale mathematics that can impact our profession and society. The numerous application drivers, ranging from biotechnology, to nanotechnology, to energy topics (renewables, materials' selection, distributed and portable generation, energy efficiency) render multiscale modeling a cross-cutting pillar of our scientific portfolio. While multiscale models now exist, development of the underlying mathematics for modeling and uncertainty quantification and of experimental protocols for design and control of emergent materials still remains elusive.

In the leap from method development to cutting-edge scientific and engineering problems, we have to deal with emergent behavior, complexity, combinatorial explosion in models and parameters, and uncertainty. Chemical engineering has been founded on our ability to simplify matters in order to solve intractable problems in a reasonable time-frame and subsequently assess and improve assumptions as deemed necessary. In this regard, coping with emergent behavior, complexity, and combinatorial explosion in models and parameters demands a similar hierarchical philosophy and offers an unprecedented opportunity for chemical engineers, computer scientists, and applied mathematicians. Successfully meeting this challenge needs training of the future workforce in a truly collaborative research setting that brings together and unifies physical chemistry, computational expertise, applied mathematics, and experimentation across all scales.

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